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A STUDY OF FIBROMYOMAS OF THE UTERUS WITH RESPECT TO THE ENDOMETRIUM, MYOMETRIUM, SYMPTOMS, AND ASSOCIATED PATHOLOGY*

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IN ANY study of fibromyomas the primary consideration should be that of the etiology of these tumors. At the present time there are several theories which merit consideration. Robert Meyer[1] propounded the idea that the appearance of myomas represents a thickening of the already present muscle bundles which are directly connected with the normal uterine musculature. De Snoo[2] developed the contention that the origin of fibromyomas is in the undifferentiated cells which he termed the genitoblasts. Embryologically the uterus proper is derived from these cells, some of which remain dormant in their embryonic state to become active in providing the material for the growth of the uterus during pregnancy and for the regeneration of the endometrium during the puerperium. Under certain conditions abnormal stimuli transpose these latent genitoblasts into fibromyomas, adenomyomas, and endometriomas. A third hypothesis is based upon the conjecture that the walls of blood vessels provide the tissue from which fibromyomas are fashioned. Graves[3] theorized that the production of these tumors is a process somewhere between true physiologic hypertrophy and actual neoplastic formation.

*Read before the Chicago Gynecological Society, January 17, 1936.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

Somewhere in the foregoing maze of evidence probably lies the answer to the etiology of the primary focus for the production of the fibroid tumors, but we must search further to find the factors that might be responsible for the stimulation of the "seed" fibroids to produce tumors of appreciable size. Pregnancy has long been considered an important element in the energizing process that brings size to fibromyomas because of the increase in thickness of the uterine muscle fibers and the markedly exaggerated blood supply to the pelvis that acts as a nourishing agent for incipient aberrant growths. By the same process of increasing blood supply, pelvic infections are deemed to be of importance as stimulators of tumor growth. More recently Witherspoon[4-7] has stated that the most active of the exciting causes is the endocrine factor. By dint of much study and interpretation he has developed the hypothesis that hyperestrinism is the main, if not the sole, agent responsible for the growth of fibromyomas. His evidence makes much of the frequent occurrence of fibroid tumors in association with cystic oophoritis (microcystic disease of the ovary) and pelvic infection, conditions in which the circulating estrin reserves are greatly increased over the normal because of the failure of follicle rupture. If such an idea is correct, it would dovetail very nicely with the previously mentioned possible stimulating factors (pregnancy and pelvic infection), since in both instances there is, besides the increased blood supply, a great increase in estrogenic hormone content.

With the advent of the study of fibromyoma stimulation by estrin, Witherspoon made attempts to associate the production of such tumors with the appearance of hyperplasia of the endometrium, adenomyosis and endometriosis on a similar endocrine basis. In view of these factors we undertook this study in an attempt to aid in clarifying this situation and to make a correlation between these pathologic entities and the clinical histories in a series of cases. The present report embraces a group of unselected patients with uterine fibromomas, studies being made upon 100 women, 69 white and 31 colored.

GROSS PATHOLOGY

A résumé of the gross pathology present in this group of women will prove of interest and may be of value in our final analysis and summation. The size of the tumor present varied from that only slightly larger than normal to the proportion of a full-term pregnancy, the size being distributed as follows:

SIZE OF TUMOR	WHITE	COLORED
6 to 8 weeks' pregnancy	38	4
3 to 6 months' pregnancy	30	20
Over 6 months' pregnancy	1	7

Since salpingitis must be kept in mind as a possible factor in the supplying of estrin excesses, we must tabulate the numbers of patients in whom this type of pathology was present. This group includes all types of tubal involvement (chronically thickened and clubbed tubes, hydrosalpinx, pyosalpinx, hematosalpinx, pseudofollicular salpingitis, and tuboovarian abscess). Evidences of these types of inflammation were found in 3 of the white women and 26 of the colored. Cystic oophoritis was present in 8 of the colored women but in none of the white. Cystic oophoritis without salpingitis was found in 5 of the white women and in no colored woman.

Of the other pelvic pathologic conditions encountered in conjunction with the fibromyomas, laceration, erosion, and infection of the

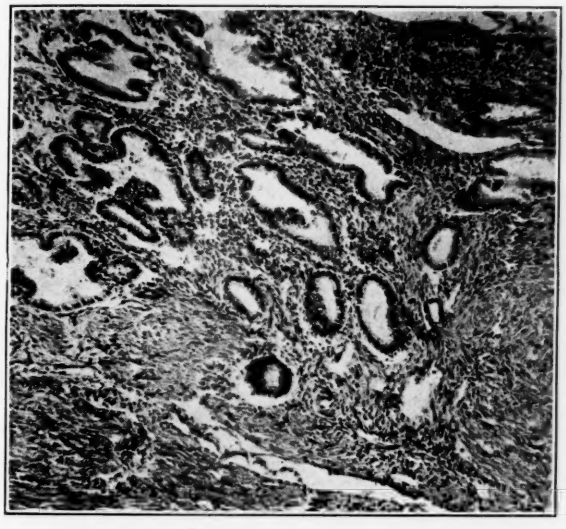

Fig. 1.—Subbasal adenomyosis.

cervix was present 12 times, vaginal relaxations 7 times, external endometriosis 9 times, endometrial polypi 6 times, prolapse of the uterus 3 times, papillary cystadenoma of the ovary twice, and each of the following once: carcinoma of the body of the uterus, lymphogranuloma inguinale, acute appendicitis, dermoid cyst of the ovary, bartholinian cyst, and pregnancy.

MICROSCOPIC PATHOLOGY

At this point it is wise to define the terms we apply to the various microscopic pictures encountered in order that misunderstanding be avoided.

Adenomyosis.—An invasion of endometrial glandular structures into the myometrium.

Subbasal Adenomyosis.—The presence of glands from the basal layer lying deep in the uterine musculature (Fig. 1). These glands are always in the proliferating stage and do not take part in the menstruating function.

True Adenomyosis.—True adenomas containing all elements of the endometrium found in definitely circumscribed areas deep in the uterine wall (Fig. 2). These tumors menstruate parallel to the endometrium and may, therefore, be found in any stage in the menstrual cycle.

External Adenomyosis or Endometriosis.—True adenomas, such as described above, situated outside the uterine cavity or myometrium, e.g., chocolate cysts of the ovary, free upon the uterine serosa, on the external surfaces of the ovaries, tubes, bowel, or in the rectovaginal septum.

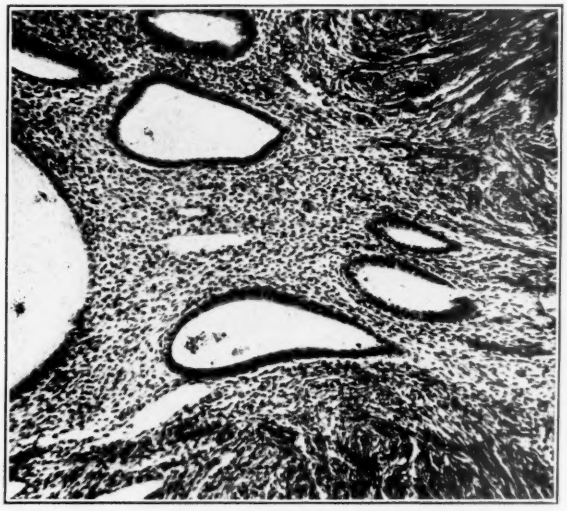

Fig. 2.—True adenomyosis.

Internal Adenomyosis was found to be present 44 times in the white women and 8 times in the colored. Of these, 30 white women and all 8 of the colored women had subbasal type of adenomyosis while 14 of the white patients displayed the true type. External adenomyosis (endometriosis) occurred 9 times among the white women and was entirely absent in the colored. Of this group 3 had chocolate cysts of 1 or the other ovary and the remaining 6 had the type that is distributed on the surface of the uterus, ovaries, etc.

The most striking feature of the study of the endometrium proper in these cases was the lack of uniformity in the thickness of the endometrium, all degrees and types of hyperplasia being found under varying conditions of associate pathology. Our criteria for hyperplasia of the endometrium are the same as those described by Cullen[8]

and Novak and Martzloff.[9] Following this classification, we found 53 patients who demonstrated the presence of endometrial hyperplasia as follows:

TYPE OF HYPERPLASIA	WHITE	COLORED
Glandular	20	7
Interstitial	4	10
Swiss cheese	4	1
All combined	3	1
Polypoid	3	0

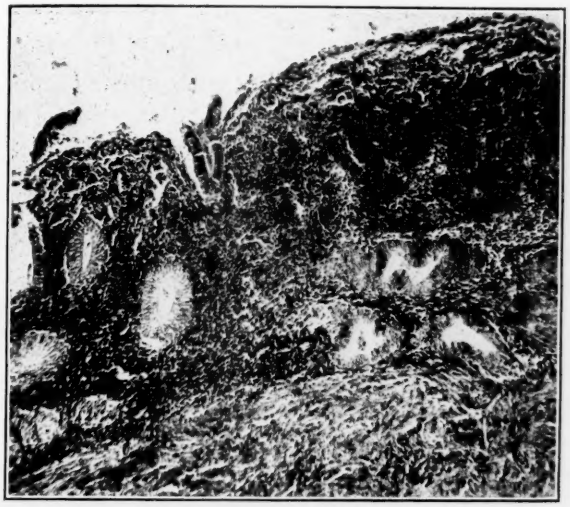

Fig. 3.—Dilatation of basal glands in menopausal endometrium.

Fig. 4.—Atrophy and hypertrophy of the endometrium.

Two distinct types of endometrial atrophy were noted during the course of this study, the true menopausal type with narrowed endometrium, few glands, and occasionally dilated glands in the basal layers (Fig. 3), and the atrophy seen in actively menstruating women with fibromyomas, the areas of endometrium lying directly over a

submucous tumor showing atrophic changes, while that in other places was normal or hyperplastic (Fig. 4). We found 24 of the women in this series displaying menopausal atrophy of the endometrium, 7 showing dilatation of the glands in the basal layer and 17 showing absence of such glandular dilatation. There were 3 patients in whom non-menopausal atrophy was evident.

True endometritis with round cell and plasma cell infiltration of the endometrial tissue was present in 3 of the colored patients. Edema of the endometrium was noted 29 times, 17 in the white and 12 in the colored patients. An interesting observation was that in some instances, although we were dealing with a proliferating stage endometrium, there existed a very definite capillary dilatation with infiltration of blood into the endometrial stroma. Such a situation prevailed 17 times in this group, 11 among the white patients and 6 in the colored.

For purposes of completeness, it was thought advisable to classify the patients in this series according to the stage in the menstrual cycle at which the endometrium was removed for study. The following table divides the women into their various groups:

Early proliferating stage	25
Late proliferating stage	9
Early secretory stage	23
Late secretory stage	31
Menopausal	12

A study of the fibromyomas themselves revealed that in 20 instances changes had taken place in their microscopic structure. Eleven showed hyaline degeneration, 6 early necrobiosis, 2 edema, 1 sarcoma, and 1 lymphangiectatic degeneration.

Since the cardinal symptoms of fibromyomas have for a long time been taught to be menorrhagia, dysmenorrhea, and leucorrhea, it was felt that a correlation of these symptoms with the location of the tumors in the uterus and the presence of adenomyosis might prove of interest. The following tables express these correlations most adequately:

	WHITE	COLORED
Menorrhagia:		
Submucous fibroids	16	9
Submucous fibroids, adenomyosis	22	2
Subserous, intramural fibroids	3	2
Subserous and intramural fibroids and adenomyosis	6	1
Dysmenorrhea:		
Submucous fibroids	8	5
Submucous fibroids, adenomyosis	13	1
Subserous, intramural fibroids	3	2
Subserous and intramural fibroids and adenomyosis	5	5
Leucorrhea:		
Submucous fibroids	8	4
Submucous fibroids, adenomyosis	6	0
Subserous, intramural fibroids	1	1
Subserous and intramural fibroids and adenomyosis	1	0

Twenty-one of the patients in this group had none of the cardinal symptoms of fibroids but had such miscellaneous complaints as the knowledge of the presence of an abdominal tumor, pressure symptoms upon the bladder or rectum, gastrointestinal disturbances, feeling of weight in the pelvis, and symptoms associated with relaxed vaginal walls and prolapse.

Another interesting point may be expressed in a study of the following table which brings out the relationship between the presence of menorrhagia and the size of the tumors encountered (Table I).

TABLE I

SIZE	WHITE		COLORED	
	MENORRHAGIA	NO MENORRHAGIA	MENORRHAGIA	NO MENORRHAGIA
6 to 8 weeks' pregnancy	25	13	1	3
3 to 6 months' pregnancy	20	10	12	8
Over 6 months' pregnancy	1	0	4	3

Although our study revealed only three women in this group who had a definite complaint of sterility, a résumé of the parity of the patients here presented may be worth noting. Of the nulliparous women in this list, four were unmarried (Table II).

TABLE II

GRAVIDA	PARA	NUMBER
0	0	35
i	0	4
i	i	13
ii	0	4
ii	i	5
ii	ii	22
iii	0	1
iii	ii	2
iii	iii	7
iv	i	1
iv	ii	1
iv	iii	1
iv	iv	2
v	iv	1
vi	iii	1

The age incidence in this group might also prove of some interest, the ages ranging from twenty-three to fifty-three years (Table III).

TABLE III

AGE	WHITE	PERCENTAGE	COLORED	PERCENTAGE
Under 25 years	1	1.4	3	9.6
25 to 35 years	6	8.7	9	29.0
35 to 45 years	37	53.5	13	42.0
Over 45 years	25	36.4	6	19.4

DISCUSSION

An analysis of the statistical data presented above may throw some light on the various factors which have been credited with providing inertia for the growth of fibromyomas. Witherspoon and other authors have brought to our attention the relative frequency of the simultaneous presence of fibromyomas, adenomyosis, and hyperplasia of the endometrium. This, together with the large number of patients in his series displaying cystic oophoritis and salpingitis, strengthened his hypothesis of hyperestrinism as the important etiologic factor in the stimulation to growth of fibromyomas. A correlation of our findings will be undertaken in an effort to evaluate this theory.

The frequency of cystic oophoritis in our series is much less than that found by Witherspoon[4] and Häggström,[10] this group having only a 13 per cent incidence discoverable grossly or microscopically. Salpingitis was present in twenty-six, or 83.8 per cent, of the colored women and only three, or 4.33 per cent, of the white. It must be remembered that 100 per cent of these patients had uterine fibromyomas while 63.7 per cent of the white women and 25.8 per cent of the colored showed evidences of adenomyosis, either the subbasal or true types, and 13 per cent of the white women had external adenomyosis (endometriosis), this latter entity being entirely absent in the colored patients studied. Hyperplasia of the endometrium was present in 53 per cent of our patients, 49.1 per cent of the white women and 60.6 per cent of the colored showing evidence of this type of pathology.

Witherspoon, after studying a group of colored women who had almost 100 per cent salpingitis and cystic oophoritis in association with fibromyomas, claimed that the pelvic inflammatory process brings an increased blood supply to the pelvis, producing an increased ovarian activity with hyperestrinism. The atretic follicles thus produced defeat the possibility of corpus luteum formation and an excess of estrogenic principles results. This may be a factor in the production of fibromyomas in the colored patients in this series, the majority of whom had coexisting salpingitis, but Witherspoon further deduces that the same etiologic factors are active in producing adenomyosis, a condition that was relatively rare in our colored patients but common in the white women who had no evidences of pelvic inflammatory disease. This becomes increasingly difficult to understand since the colored women had, as a rule, larger tumors, a fact that would suggest a greater excess in the circulating active estrin content.

Again, if hyperplasia of the endometrium can be taken as a criterion of excessive estrin stimulation, one would expect to find more than a 53 per cent incidence in a series of patients with fibromyomas. In postmenopausal patients with theca or granulosa cell tumors of the ovary, bleeding from the uterus is frequently encountered. These

patients have a hyperplasia of the endometrium as a result of the hyperestrinism produced by or in the tumor. Since hyperplasia of the endometrium is induced by estrogenic principles in the presence of these ovarian neoplasms in patients who have passed the climacteric, it is difficult to understand the comparatively large number of postmenopausal patients in the present series having endometrial atrophy of the menopausal type in the presence of fibroids which are products of estrin stimulation.

Some observers make much of the absence of corpora lutea in the presence of fibromyomas on the theory explained above. Häggström found many ovaries in his series to contain these bodies in various stages of development and retrogression. In our group nine patients showed the presence of corpora lutea, recent or old, in the ovaries removed, and, if we may be allowed to presume, there were probably many more in the ovaries left in situ which were not mentioned in the operative records.

A study of the symptomatology gives rise to some interesting thoughts. There were 61 patients in this series who had menorrhagia; 49 of these had submucous fibromyomas with or without adenomyosis and 12 had subserous and intramural tumors. If the estrogenic factor is so potent as to produce hyperplasia of the endometrium with a resultant bleeding in elderly women with hormone producing tumors of the ovary, we are forced to inquire as to why the same stimulus that produces the fibroid tumors does not develop menorrhagia in more than 61 per cent of our patients.

The estrogenic principle is the active motor stimulant for the uterine musculature and some workers attempt to explain dysmenorrhea seen in patients with fibromyomas on a hyperestrin basis, the excess of this hormone providing for vigorous uterine contraction unopposed by progestin because of the suppression of the corpora lutea. In our group 42 patients complained of pain associated with the menstrual periods. Of this number, 27 had submucous fibromyomas, 15 had subserous and intramural tumors and 14 had salpingitis, which factor alone is frequently responsible for dysmenorrhea because of the pelvic and bowel adhesions resulting from this type of pathology. Looking deeper into this symptomatic element, it can be seen that the majority of patients with menorrhagia and dysmenorrhea had submucous fibromyomas, while a lesser number displayed subserous and intramural growths. We feel with Häggström that the location of the tumors with respect to their proximity to the uterine cavity is a more logical explanation for the menorrhagia and dysmenorrhea, the bleeding resulting from a constant endometrial hyperemia induced by the tumors directly underlying and crowding the endometrium and the dysmenorrhea as a product of vigorous uterine contraction in an attempt to expel the

foreign bodies (tumor masses) lying in or near its cavity. By the same token patients with very large subserous and intramural fibromyomas which may reach full-term pregnancy proportion are lacking in these symptoms.

A survey of the obstetric histories in this group shows that there was sterility in forty of the women, four of the nulliparas having been unmarried. Still, we are dealing with a series of patients in whom salpingitis of one form or another with tubal closure was present twenty-nine times, a fact accounting for some of the lack of pregnancy. Again, we must disagree with Witherspoon's contention that the sterility associated with fibromyomas is explained totally by the hyperestrinism he believes is produced by the atretic follicles in the absence of corpora lutea. We cannot believe that a great number of the sterilities in this group can be explained upon a basis of estrogenic excess because of the small number of our patients displaying atretic follicles and because of the occasional presence of corpora lutea.

SUMMARY

A study of the uterine walls, ovaries, and endometria in a series of 100 patients having fibromyomas with a correlation between these findings and the clinical histories and symptoms, still gives us no definite basis upon which to make an absolute statement as to a single etiologic or stimulating factor in the production of fibromyomata uteri, adenomyosis externa or interna, and hyperplasia of the endometrium with resultant menorrhagia, dysmenorrhea, or sterility.

Evidence in favor of Witherspoon's theory making hyperestrinism the single activator in the production of these pathologic and clinical entities, can be found in the observation of the rapid growth of fibromyomas during pregnancy and their puerperal and menopausal regression. Such facts follow very closely the estrin levels now well established, as does the discovery of hyperplasia of the endometrium associated with the presence of theca and granulosa cell tumors of the ovary in women who have passed the menopause.

We have presented in our discussion factors that may tend to oppose this theory, at least in part. We must, therefore, feel with Witherspoon that hyperestrinism plays a part in the production of the changes herein studied and discussed, but we cannot be convinced that it is the sole agent because of the lack of consistency in the finding of other pathologic and symptomatologic entities in association with fibromyomas.

The logical conclusion that can be derived from this study is that fibromyomata uteri, endometriosis, adenomyosis uteri, and hyperplasia of the endometrium with associated menorrhagia, dysmenorrhea, and sterility cannot be traced to a single etiologic agent but appear to be products of various and varying factors.

REFERENCES

(1) *Meyer, Robert:* The Pathologic Anatomy of the Uterus, Chap. 7, p. 213. (2) *De Snoo:* J. Obst. & Gynec. Brit. Emp. **41**: 568, 1934. (3) *Graves, William P.:* Uterine Myomata. In System of Obstetrics and Gynecology by Curtis, Philadelphia, 1933, W. B. Saunders Company **2**: p. 745. (4) *Witherspoon, J. Thornwell:* Endocrinology **17**: 703, 1933. (5) *Idem:* Surg. Gynec. Obst. **56**: 1026, 1933. (6) *Idem:* Surg. Gynec. Obst. **58**: 57, 1934. (7) *Idem:* Surg. Gynec. Obst. **61**: 743, 1935. (8) *Cullen, Thomas E.:* Cancer of the Uterus, New York, 1900, D. Appleton and Company, p. 479. (9) *Novak, Emil, and Martzloff, Carl H.:* Am. J. Obst. & Gynec. **8**: 385, 1924. (10) *Häggström, Paul:* Ztschr. f. Geburtsh. u. Gynäk. **102**: 36, 1932.

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DISCUSSION

DR. HAROLD O. JONES.—I believe that hyperplasia of the endometrium is a term that is often very carelessly used. Certainly the sections thrown on the screen could be classified as different phases of cyclic manifestation. I have the same criticism of Witherspoon's work and do not believe that he is justified in making comparisons unless sections from both ovaries are available for study of the corpus luteum.

DR. RALPH A. REIS.—Dr. Baer, Dr. DeCosta, and I undertook a study similiar to this one of one thousand consecutive patients at Michael Reese Hospital, two or three years ago. Although Witherspoon found salpingitis in almost 100 per cent of his series, we found it in only 19.4 per cent, which is even lower than Dr. Kanter's figures. These variations are probably due to the differences in the social, economic, and racial status of these series of patients. We found also very little sterility, over 80 per cent of our patients having been pregnant one or more times. In patients who were sterile, there was a 31 or 32 per cent incidence of salpingitis, whereas in those who had had children the incidence was only 7 per cent. We thought, therefore, that the sterility was due to associated salpingitis and not due to the fibroid.

We have tried to be very rigid in our description of hyperplasia of the endometrium and accordingly found hyperplastic endometrium in less than 18 per cent of the patients whose uteri were examined. The lack of symptoms in as large as 30 per cent, as Dr. Kanter reported, corresponds with our figures of 32 per cent which showed neither bleeding nor pain nor increase in menstruation.

DR. AARON E. KANTER (in closing).—I expected a little controversy about what is to be considered hyperplasia. That is the reason I stated what stage of the endometrium we studied. I believe that dilated glands of varied sizes, especially with duplication of glands, is not a normal finding. Some of the slides shown tonight were hyperplasia but it is difficult to state the type.

We have not tried to bring out conclusively the cause of fibromyomas, but we do not believe it is an excessive amount of estrogenic hormone in the system.

Huffman, J. W.: Trichomonas Vaginalis Vaginitis, Am. J. Surg. 30: 312, 1935.

This is a preliminary report on 14 patients suffering from vaginitis, associated with *Trichomonas vaginalis* infestation, who have been treated with iodochlorhydroxyquinoline. The use of this product appears more satisfactory in this group than any other previously tried method. In the patients under observation there have been no recurrences up to five months.

J. Thornwell Witherspoon

SOME POINTS IN THE TREATMENT OF ENDOMETRIAL HYPERPLASIA BY PROGESTERONE THERAPY*

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THE treatment of menstrual disorders and ovarian dysfunction by methods of ovarian organotherapy has in the past been notoriously unsatisfactory and inefficient. This has been due to a variety of reasons. Lack of knowledge of the exact processes involved was, of course, an important factor. Furthermore, the various ovarian preparations used for therapeutic purposes could not be anything but ineffectual in securing the desired results. We now know that extracts of the corpus luteum, ovarian residue, and such, when given by mouth, are practically valueless, while those formerly administered by hypodermic injection contained little or none of the potent hormones.

The isolation and purification of the two important ovarian hormones, estrin and progesterone, have led to renewed hopes from the therapeutic standpoint. True, our knowledge of ovarian function has advanced greatly, and the nature and function of the ovarian hormones are better understood, so that it is possible now to approach the study of patients presenting menstrual abnormalities in a more logical manner, and in some instances at least to offer more rational treatment than has hitherto been possible.

At the same time we would emphasize that the indiscriminate injection of ovarian hormones in the treatment of menstrual disorders can result only in many bitter disappointments. In considering the two ovarian hormones, estrin and progesterone, it must be recalled that while the action of progesterone succeeds and is complementary to that of estrin in the normal cycle, at the same time the effects of the two are also antagonistic to each other to a degree. These facts can be taken advantage of in ovarian therapy, and the relations between the two must be constantly kept in mind if we wish to treat our patients on rational lines. For example, in the patient whose ovaries are already producing an oversupply of estrin, it would be most illogical to administer more of the already too abundant hormone, while on the other hand, in the case of an underproduction of progesterone, this can be compensated for only by the administration of progesterone and not estrin.

*Read, in part, by invitation, before the New York Obstetrical Society. February 11, 1936.

It is not our purpose here to go into the whole question of ovarian therapy but rather to emphasize some points which have developed in the treatment of a group of patients by progesterone therapy. This group includes several women presenting themselves on account of persistent and profuse uterine bleeding, in whom, after curettage, the typical microscopic picture of endometrial hyperplasia was revealed. The basis for this type of benign bleeding would appear to lie in the failure of ovulation to occur and the consequent failure of the corpus luteum to develop. There is thus probably a persistent estrin activity with little or no production of progesterone. This group would, therefore, appear to be logical subjects for progesterone therapy in the hope of supplying their deficiency. As the fundamental factor is the failure of ovulation to occur, a still more logical treatment would be the administration of the ovulation-stimulating hormone of the anterior pituitary, which is clinically not yet possible.

The first difficulty encountered in progesterone therapy is the estimation of the dosage to be used. Unfortunately there is at present no satisfactory means available for determining the progesterone content of the blood in small amounts. Furthermore, although it is possible to determine the progesterone content of corpora lutea in the laboratory, we are entirely ignorant of the amount of hormone produced daily during the period of activity of a particular corpus luteum. Consequently, although we may recognize that in the given case there is deficient production of progesterone, we have no means available for learning what the deficit actually is. For this reason the initial dosage used can only be decided empirically, the dosage being increased or decreased, or the treatment continued or suspended according to the results obtained.

The following examples of uterine bleeding associated with endometrial hyperplasia are presented in some detail as they illustrate certain particular points in connection with progesterone therapy in this type of bleeding. The progesterone used was the purified hormone prepared from sows' ovaries by one of us (Elden) according to the method of Allen and Meyer, the hormone being then dissolved in sesame oil, and standardized.*

CASE 1.—E. C. (Unit 11752), aged forty-six, para i. The patient was admitted in June, 1933 after several weeks of rather persistent bleeding, at times moderately profuse. Diagnostic dilatation curettage June 16, 1933; curettings showed a moderate degree of hyperplasia. Following dilatation and curettage there was normal menstruation for five months, then she began to have persistent slight bleeding, the amount never great but became of such a nature that there were only two or three days free from bleeding in each month. Antuitrin-S was tried on several occasions without success. Total period of this slight bleeding was one year. She had associated sinus headache. Radiation therapy or hysterectomy was being

*One rabbit unit corresponds to 1 mg. of the purified crystalline hormone.

considered. Progesterone 1/25 Rb.U. Dec. 7, 9, 11, 1934 (total 3/25 Rb.U.). Bleeding stopped twentyfour hours later, slight recurrence for one day, then stopped entirely for twelve days, the longest period of freedom in over a year. Slight bleeding began again, increased in amount until it amounted to what was apparently a moderately profuse menstrual period, duration twelve days. Without further therapy, she menstruated quite normally, at twenty-eight- to thirty-day intervals, duration four to five days, until September, 1935 when she began to have irregular two- to three-day periods of slight bleeding in between regular menstrual periods. With establishment of regular menstruation, the previously persistent headaches disappeared and recurred only at time of menstruation. She was treated again in November, 1935 on account of recurrence of slight bleeding. She was given 2/25 Rb.U. on 3 successive days (total 6/25 Rb.U.) This second period of therapy was in turn followed by improvement and reestablishment of normal menstruation.

CASE 2.—R. A. (Unit 45142). This patient was first admitted on Nov. 16, 1931, at the age of sixteen years. At the age of thirteen, one year after onset of menstruation, she began to bleed persistently and almost daily up to the time of this admission, usually slight but at times quite profuse and for the past two months constant, rather free bleeding. Secondary anemia, Hb. 70 per cent. Dilatation and curettage Nov. 19, 1931, typical hyperplasia. Dilatation and curettage was followed by 3 small x-ray treatments (105 m.a. each, ovaries, spleen, pituitary). She was slightly relieved by above treatment, but in a few months there was a recurrence of bleeding, usually not profuse but so persistent that the free intervals were infrequent and of short duration. Readmitted Jan. 31, 1935, aged twenty, after an episode of rather profuse bleeding. Basal metabolism rate –10 per cent. Given 5/25 Rb.U. on each of 3 successive days (total 15/25 Rb.U.). Bleeding decreased second day and had practically stopped on third day. After six days' freedom from bleeding, 5/25 Rb.U. repeated three days later (total 10/25 Rb.U.) no bleeding, the last 2 doses probably unnecessary. No bleeding for slightly over five weeks, the longest interval of freedom in past four years. Slight bleeding than began and persisted, occasionally somewhat increased. After three weeks given 2/25 Rb.U. on three successive days (total 6/25 Rb.U.) flow decreased but did not stop, amount very moderate. A week later 3 doses 2/25 Rb.U. at two-day intervals. Bleeding stopped entirely and did not recur for three weeks. Slight bleeding than began May 6, 1935. Given 2/25 Rb.U. on three successive days (total 6/25 Rb.U.), bleeding stopped temporarily but recurred, and repeated 3 doses of 2/25 Rb.U. beginning three days after last series (total 6/25 Rb.U.). A very slight daily flow persisted for a total of four weeks, only on two days amounted to as much as a normal menstrual period. Given 4/25 Rb.U. on three successive days (total 12/25 Rb.U.). Bleeding stopped entirely after third dose. No bleeding for three weeks. Bleeding began again on June 24, 1935, rather free. Three daily doses 4/25 Rb.U. (total 12/25 Rb.U.). Bleeding decreased and finally stopped after three days. Thirty-one days' freedom from bleeding except for slight spotting on one or two occasions. Bleeding began again July 31, 1935, and was rather profuse. Two doses 4/25 Rb.U. (total 8/25 Rb.U.); did not report for other dose. Flow decreased but increased markedly a week later, given 2 doses 6/25 Rb.U. (total 12/25 Rb.U.); flow stopped six days later; duration of flow sixteen days. No bleeding for thirty days, followed by free flow for ten days, given 4 doses (4/25 Rb.U., total 16/25 Rb.U.). Flow checked after second injection but persisted for several days more before stopping entirely. This patient presented difficulties in regularity of treatment. She felt so much better than at any time in the previous four years that she became at times rather perfunctory in reporting symptoms. No treatment given since September, 1935. No bleeding in October except for very slight flow

for about an hour on 2 occasions. Began to flow Nov. 1, 1935, duration one week, very profuse for three days. Nothing in the way of a regular period in December, but has had slight bleeding for part of a day on three occasions.

CASE 3.—N. G. (Unit 98540), aged eighteen, single. The patient was admitted in January, 1935 on account of excessive menstruation. Menstrual onset at age of twelve, and quite normal for first four years. Since pneumonia two years ago menstrual periods totally irregular at four-to fourteen-day intervals, scanty in amount and of variable duration from two to eight days. Had received thyroid therapy from family physician, amount unknown. Had gained 10 pounds in weight in past five months. Physical and pelvic examinations essentially negative, the only significant finding being a basal metabolism rate of −16 per cent. Dilatation and curettage Jan. 31, 1935 showed typical endometrial hyperplasia. Following dilatation and curettage given $\frac{3}{25}$ Rb.U. of progesterone weekly for three weeks (total $\frac{9}{25}$ Rb.U.), also ½ gr. of thyroid daily. No bleeding for two months, then had apparently normal menstrual period lasting six days. For four months was given $\frac{3}{25}$ Rb.U. of progesterone in last half of each twenty-eight-day cycle, 4 normal periods occurring after this treatment.

All therapy then was suspended and for past three months there had been no bleeding of any kind. Associated with this amenorrhea she developed symptoms of a mild hypothyroidism, and a recent basal metabolism rate gave a reading of −21 per cent. She is at present receiving thyroid therapy, 3 normal menstrual periods resulting, the last, January, 1936.

CASE 4.—B. A. (Unit No. 79071), aged nineteen, single. The patient was admitted on Aug. 22, 1933 on account of vaginal bleeding. Menstrual onset at age of thirteen, irregular and scanty for three years followed during the next two years by more normal menstrual flow though somewhat irregular. Beginning a year before admission, duration of menstrual period fourteen days, and for past six months bleeding has been almost constant. Has lost 40 pounds in weight in past year by dieting, present weight 73.2 K. General physical and pelvic examinations essentially negative. Laboratory findings showed an R.B.C. of 2,760,000; Hb. 55 per cent; W.B.C. 6,100. Basal metabolism rate −1 per cent. Blood chemistry normal; galactose tolerance test normal. Dilatation and curettage Aug. 26, 1933, typical endometrial hyperplasia. Treated for next three months by anterior pituitary gland given in salol coated capsules at theoretical time of ovulation with no benefit. Injection of 200 units of antuitrin-S was also done without benefit; irregular and persistent bleeding continued. Second dilatation and curettage Dec. 9, 1933, typical endometrial hyperplasia. Given a total of 10 Rb.U. progesterone in three days just after theoretical time of ovulation, and this was repeated at the same time and in the same amount in 2 succeeding cycles. Three periods of bleeding (menstrual?) occurred, rather profuse and of six to seven days' duration, no bleeding between these periods.

A control period now started with no therapy. No bleeding of any kind for two months followed by a normal period of six days' duration. Two weeks later began to bleed again and this continued for twenty-four days. Two normal periods occurred in the succeeding two months. For the next four months, the periods were irregular, profuse, and when not bleeding actively, there was almost daily "spotting." Several endometrial biopsies taken during the control period showed no premenstrual changes. Urinary estrin studies showed varying amounts of estrogenic substance from 0 to 32 Rb.U. daily.

Third dilatation and curettage on Feb. 24, 1935. Following this operation, she was given small doses, $\frac{3}{25}$ Rb.U., of progesterone at weekly intervals during the last half of her menstrual cycle, and this was continued for the next eight months.

Menstrual periods have been regular to within a day or two, while the duration and amounts of flow have been normal. Treatment stopped in October, 1935. After two essentially normal menstrual periods, began to "spot." Progesterone 3/25 Rb.U., weekly, has apparently again brought the situation under control.

CASE 5.—B. B. (Unit No. 93258), aged thirty-two. The patient had a spontaneous miscarriage at six months three years ago. Dilatation and curettage August, 1934 on account of menorrhagia, moderate hyperplasia, followed by period of relief. Recurrence of menorrhagia in March, 1935 increasing in amount and duration; periods regular but very profuse and lasting six to seven days. Progesterone therapy began in June, 1935. Two doses of 2/25 Rb.U. on two successive days before onset of periods each month since that time have resulted in periods of normal duration and amount.

In addition to the foregoing patients whom we have observed for considerable periods of time, a number of others have been treated for shorter periods of time. Some of them may apparently be regarded as successes though the period of observation has been too short to be assured of this. There have also been a number of failures. These latter we are inclined to attribute to either too small dosage or to improperly timed dosage. We hope to present a more complete series at a later date.

DISCUSSION

The results obtained in the treatment of these five cases of vaginal bleeding can be regarded as satisfactory, but the mechanism, by which these results were brought about, is not so clear. These patients presented varying degrees of uterine bleeding and were treated on the assumption that their own production of progesterone was deficient. As mentioned above, it is at present impossible to determine the degree of deficiency of progesterone production in the individual, consequently the dosage administered has been determined on empirical lines. The small dosage was selected for no particular reason except as a starting point.

Case 1 presents an extraordinary result obtained from a very small dosage of progesterone. The immediate effect so far as the bleeding was concerned was striking enough, but of still more interest was the ensuing period of normal menstruation without further therapy. One can only speculate as to the mechanism by which this was brought about. It might appear that the small doses of progesterone were in this instance sufficient to bring about a balance between the estrin and progesterone production on the part of the organism and that that balance once restored was maintained by the organism for a period of several months. That the result obtained was not a matter of simple coincidence is demonstrated by the fact that the slight recurrence of symptoms nine months later was again controlled by the same therapy with small doses of progesterone.

In Case 2 the situation was somewhat different, repeated administration of progesterone being necessary from time to time to control the bleeding, and also somewhat larger doses were found to be necessary to bring about the desired result. As will be seen above in her case history, while small doses totalling 6/25 Rb.U. of progesterone caused a decrease in the bleeding, usually 12/25 to 15/25 Rb.U.

were necessary to bring about complete control. The picture here is more nearly what one would expect in frank substitution therapy. The end-result and her behavior during three months without any therapy suggest that for the time being at least a proper balance between estrin and progesterone production may have been established.

In Case 3 we are dealing with the combination of uterine bleeding associated with endometrial hyperplasia and also a very definite hypothyroidism. The beneficial results of progesterone therapy are seen in the 5 normal menstrual periods which occurred after its use preceding each period. This in turn has been succeeded by very definite signs of hypothyroidism.

Case 4 presents still different aspects. Following treatment with large doses of progesterone, some tendency toward periodicity was established, but the three periods, thus treated, were profuse and of longer than normal duration. This effect is difficult to explain, and we can only speculate on the mechanism by which the effects were produced. The results were certainly not as striking as in the preceding cases with the administration of smaller dosage, and in this patient too the situation was brought under control later by the repeated administration of small doses of progesterone. Possibly the latter procedure more nearly simulates the normal situation in the body in regard to progesterone production.

Case 5 may be regarded as an example of severe menorrhagia controlled, though as yet not cured, by progesterone therapy.

It is obviously impossible to draw any sweeping conclusions from the above series, and no attempt will be made to do so. From the results obtained, however, it would appear that treatment by progesterone therapy may well be given serious consideration in the treatment of uterine bleeding associated with endometrial hyperplasia when there is presumably a deficient production of progesterone on the part of the ovaries. If and when it shall become possible to determine how much of the hormone is necessary for normal function and to determine how much is produced by the individual in a given case, it will then be possible to determine the dosage according to the deficit which exists. For the present, however, the dosage will have to be along empirical lines until we learn in a given case, by the method of trial and error, the amount necessary to establish equilibrium. Another fact to keep in mind is the fact that solutions in oil are absorbed slowly. Consequently no immediate effect would be expected: at least twenty-four to forty-eight hours must elapse. This is of importance in arranging the time of administration of the hormone.

The dosage in our patients has been very small when compared with the dosage found necessary for frank substitution therapy in experimental work. Thus, Allen and Corner found it necessary to administer 1 Rb.U. per day to maintain pregnancy in the castrated rabbit. Kaufman, in an interesting experiment on a castrated woman, found it possible to reproduce a premenstrual endometrium followed by bleeding only after the administration of 50,000 rat units of progynon followed by 35 rabbit units of progesterone. Elden, repeating his experiment, failed to bring about similar changes through using the

same dosage of ovarian hormones. All these experiments indicate the large amounts of ovarian hormones necessary for frank substitution therapy, and the small dosages used in our patients obviously do not fall in that category. Kaufman has also had success in treating patients similar to ours with relatively small doses of progesterone, 5 to 10 rabbit units extended over five-day periods, though his dosage is somewhat larger than we found necessary.

The explanation of the results obtained is not clear, and we can only theorize as to how they were brought about. Obviously with the ovaries in situ, the situation is quite different from that of the castrated woman.

Possibly a certain amount of progesterone is produced even in the absence of ovulation in follicles undergoing atresia. Or possibly the effect produced by these small doses is an indirect one on the cycle through the medium of the pituitary rather than from any direct effect on ovaries or uterus. The question cannot be answered at the present time but offers an interesting problem for future investigation.

SUMMARY AND CONCLUSIONS

The results obtained in five women presenting uterine bleeding associated with endometrial hyperplasia and treated by progesterone therapy are presented. In this small series the results may be regarded as satisfactory, but they are also presented on account of the problems arising in connection with the determination of the proper dosage to use, which for the present must be along empirical lines, as well as the possible explanation of the results obtained. The correlation of the appearance of the endometrium with the therapy, by means of frequent biopsies, would have been highly desirable, but unfortunately it was not feasible.

REFERENCES

Allen, W. M., and Corner, G. W.: Proc. Soc. Exper. Biol. & Med. **27**: 403, 1930. *Allen, W. M., and Meyer, R. K.:* Am. J. Physiol. **106**: 55, 1933. *Elden, C. A.:* Endocrinology **20**: 47, 1936. *Kaufman, C.:* Zentralbl. f. Gynäk. **56**: 2058, 1932. *Idem:* Proc. Roy. Soc. Med. **27**: 849, 1934. *Idem:* J. Obst. & Gynec. Brit. Emp. **42**: 409, 1935.

Walker, R. Milnes: Undescended Ovaries, Lancet 2: 1346, 1935.

The author reports his second case of undescended ovary. The usual symptom is pain which is localized at the area of attachment. In this case the pain appeared to result from the spill of blood. The location is likely to be in the iliac fossa but may be higher. The gonad is prone to be covered by the colon but may lie laterally to it.

There is no need to remove the ovary, but its nerve supply should be severed.

H. Close Hesseltine.

CERVICAL DILATATION IN DRY LABOR AND AFTER DELIBERATE EARLY RUPTURE OF THE MEMBRANES*

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HOW does the cervix open, and what is the rôle of the amniotic sac in labor, are questions that have been disputed since the beginning of scientific obstetrics.

The opinion that the membranes are vital to labor goes back, according to Jacquemier,[1] to the teaching of Paré's pupil, Guillemeau, who lived in the latter half of the sixteenth century. It is also known that harsh criticism followed the pioneer daring in 1738 of Mary Donally, an English midwife, who was probably the first to induce labor by rupturing the membranes.[2] She achieved the delivery of a premature but live child through a contracted pelvis that had caused the death of two previous full-term infants. A Dr. Macaulay could not be dissuaded by a consultation of his colleagues in 1756 from the same course, which had a similar happy termination.[3]

William Smellie[4] in 1752 cautioned against rupture of the membranes, but stated: "The membranes appear to play no part in labor except to hold in the water necessary for lubrication. Dilatation is effected by the head." The then prevalent hydrostatic wedge theory was upheld by Thomas Denman[3] who in 1778 made the oft-quoted statement: "The amniotic fluid enclosed in the membranes procures the most gentle, efficacious dilatation of the os uteri." However, he admitted that "in many cases the membranes break spontaneously before the period of complete dilatation without any material inconvenience" Baudelocque[5] in 1789 held a gloomy prognosis for dry labor (even though he ruptured the membranes for induction). However, he warned the profession that "dilatation is not immediately and entirely the effect of that species of wedge." John Burns[6] at the turn of the century stated that he "could not go the length of some who say the evacuation of the waters is always hurtful for there are circumstances in which it is allowable and beneficial." But he went on to strike the first blow against "meddlesome midwifery."

In 1806 William Potts Dewees was graduated from the University of Pennsylvania. His thesis, which Howard A. Kelly quoted Shippen as saying marked a new era in the history of medicine, was "An Essay on the Means of Lessening Pain and Facilitating Certain Cases of Difficult Parturition," in which he criticized the theorizing of Denman. The following year he continued his criticism in editing Heath's translation of Baudelocque, the first textbook of obstetrics published in the United States. Shortly afterward appeared his classic *Compendious System of Midwifery.*

Dewees[7] pointed out that, if the membranes were a dilating wedge, they must be stronger than the cervix, and he compared the ease with which the membranes rupture at the slightest touch to the difficulty of manual dilatation. Again, in the absence of membranes, labor should be almost impossible or very difficult, which he found "contrary to experience" in spite of occasional exceptions.

Dewees' explanation of the "Manner in Which the Os Uteri Is Opened" is briefly that the cervix begins to lose thickness and breadth as soon as it is operated

*Read at a meeting of the Cincinnati Obstetrical Society, March 12, 1936.

upon, this in spite of the circular muscles. The longitudinal muscles contract coincident with the relaxation of the circular muscles, and the cervix is thus gradually retracted over the head.

Faced thus with two entirely different theories to explain the mechanism of the dilatation of the cervix, succeeding obstetricians hesitated to fly in the face of tradition and tried to combine the two. For example, Velpeau felt that although Dewees' explanation was correct, the waters helped "somehow" in the process, and he called for new studies on the subject. Jacquemier's textbook of 1846 considered that rupture of the membranes in no way hindered dilatation. In 1858, Sinclair and Johnston[8] noted that in 13,000 deliveries at the Dublin Lying-In Hospital, the rupture of the membranes during the first stage did not tend to delay labor, and they reported "no hesitancy in puncturing them." On the other hand, Chailly pleaded for the membranes if only as a protection to the child. Ramsbothan in England, Cazeaux in Paris, and the then rising German school ignored Dewees, and although Gunning S. Bradford taught his theory in 1861, even America, led by Hugh L. Hodge, condemned it to the place of historical interest.

Although our textbooks teach the hydrostatic wedge theory with or without minor modifications, impetus to a new study of the mechanism of the dilatation of the cervix has come from two sources: first, the increasingly popular method of inducing labor by rupture of the membranes, and second, the apparently independent evolution of the Dewees explanation, and a practical application of it, by Kreis of Strasbourg.[9]

In accordance with the hypothesis that the membranes are the dilating agent or at least the most significant element in the dilatation of the cervix, dry labor, as a corollary, should be exceedingly difficult and prolonged. With the theory of reciprocal muscle action as the dilating mechanism, the presence or absence of the membranes should be immaterial. In fact, the absence of membranes should aid labor inasmuch as the retraction of the cervix is more easily accomplished over a hard head than over a somewhat yielding mass of fluid. As a test of the validity of either of the two explanations, a very simple experiment might be devised to determine the length and difficulty of labor in relation to the integrity of the amniotic sac.

Supplementing observations reported in 1934 of the results obtained with deliberate rupture of the membranes early in labor,[10] the problem was again investigated with the material of 1,621 obstetric admissions to the Methodist Episcopal Hospital of Brooklyn during the year 1934 and 1935. To have an adequately controlled experiment all variable factors have to be eliminated. Hence, the study was limited to strictly normal parturitions by excluding the following: abortions, premature labors (to thirty-eight weeks), breech and transverse presentations, twins, hydramnios, toxemia, bleeding cases, contracted pelvis, and constitutional complications, such as tuberculosis and heart disease. It was felt wise to exclude women admitted to the hospital in the second stage of labor, as well as those whose charts contained insufficient data for proper classification. There was a fourth cause for exclusion, namely, ignorance of whether or at what time the membranes actually ruptured. In none

of the recent studies on dry labor has this been recognized, and undoubtedly the membranes were erroneously considered intact. The size of the error thus introduced is considerable. In the Woman's Clinic of the New York Hospital[11] where such a classification is made, the number of cases with time of rupture undetermined amounts to about 10 per cent. At the beginning of this experiment some 11 per cent of women fell into this group, but by the routine use of the brom-thymol-blue test during the last few months, the figure was reduced to 6 per cent.

TABLE I. CLASSIFICATION OF OBSTETRIC ADMISSIONS, METHODIST EPISCOPAL HOSPITAL, BROOKLYN, N.Y. JULY 1, 1934 TO JUNE 15, 1935

	COMBINED	PRIVATE	WARD
All obstetric admissions	1621	723	898
Abnormal cases	354 (22%)	169 (23%)	185 (20%)
Admitted in second stage	117 (7%)	54 (7%)	63 (7%)
Insufficient data	36 (4%)	22 (3%)	58 (6%)
Undetermined rupture of the membranes	91 (6%)	61 (8%)	30 (3%)
Normal Cases for Study:	1001	403	598
A. Intact membranes	404	194	210
B. Dry labor	311 (31%)	130 (32%)	181 (30%)
C. Spontaneous "partial dry"	107 (11%)	38 (9%)	69 (12%)
D. Deliberate "partial dry"	179	41	138

There were thus 1001 normal, full-term, occipitoanterior or occipitoposterior deliveries available for the experiment, as indicated in Table I. These were grouped into four classes: A, typical labor with intact membranes to the end of the first stage, that is, those cases in which dilatation of the cervix might have been accomplished by the hydrostatic wedge; B, typical dry labor, that is, those women whose dilatation was accomplished in the complete absence of the hydrostatic wedge, presumably by the reciprocal muscle action; C, termed spontaneous "partial dry" wherein the membranes ruptured spontaneously after a dilatation of from 4 to 7 cm.; D, the experimental group, women in active labor with a dilatation of from 4 to 7 cm., on whom deliberate rupture of the membranes was practiced in order to observe whether the absence of a hydrostatic wedge made any difference in the type of labor and whether there was any difference in the early and later parts of labor. For most purposes Classes C and D can be combined under the heading of "partial dry labor."

A very striking finding was the high incidence of dry labor, 31 per cent, which included, however, rupture of the membranes up to the establishment of pains at twenty-minute intervals. Williams[12] has no

TABLE II. DISTRIBUTION OF PRIMIPARAS AND OCCIPITOPOSTERIOR POSITIONS

	A	B	C, D
All cases, 1,001 (100%)	40%	31%	29%
All prim., 484 (100%)	35%	35%	30%
Prim. in each class	42%	54%	51%
All o-p's, 381 (100%)	39%	29%	31%
O-p's in each class	37%	36%	41%

statistics of his own but quotes a figure of 10 per cent. At the New York Hospital[11] the incidence in normal vertex cases is 19 per cent with another 10 per cent unclassified. Of the two conditions usually blamed for this accident, namely, contracted pelvis and occipitoposterior position, Schultze[13] showed definitely that contracted pelvis was not a factor, the nineteenth century writers to the contrary notwithstanding. Table II demonstrates that occipitoposterior position is also not a predisposing factor. On the other hand as has been pointed out by others, a tendency to premature rupture is apparently associated with primiparity.

Returning to the mechanism of dilatation of the cervix, it is apparent that, as the textbooks state, the absence of a fluid wedge should lead to

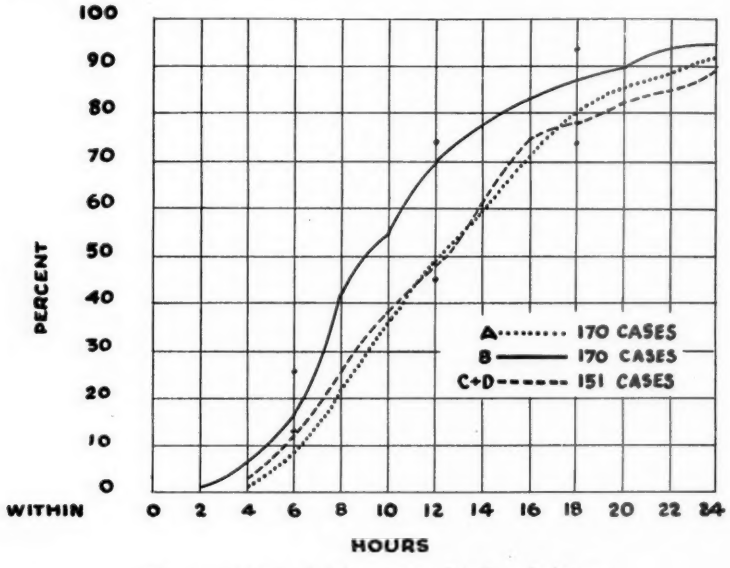

Fig. 1.—Ogive of labors completed, primiparas.

a prolonged labor. On the other hand if the amniotic sac is superfluous, or as has been suggested, occasionally even a hindrance, the reverse should hold true and with ruptured membranes there should be a smaller percentage of prolonged labors. That this was actually the case was demonstrated by Schultze[13] in 1929, who found that whereas the incidence of prolonged labor in 6,500 deliveries was 12.4 per cent, it was only 8.4 per cent in 600 dry labors; it was demonstrated again by Mason[14] in 1933 who found 10 per cent of 1,000 consecutive labors extending over twenty-four hours, whereas only 2 per cent of the dry labors were prolonged. In this experiment, 6 per cent of the control "wet labor" cases were difficult and prolonged, but only 3 per cent of the dry labor cases.

Kreis[15] has shown furthermore, in a study of nearly 3,000 cases, that at any given time there will be a larger percentage of women who have

completed the dilatation and delivery in the absence of membranes than with intact membranes. Figs. 1 and 2 show the ogive or cumulative distribution curves for primiparas and multiparas, respectively, in the 1,000 normal cases. It will be observed that when the membranes ruptured before the onset of labor, dilatation was completed faster than in the so-called normal cases, and as might be expected, the partially dry labor cases fell somewhere between the two. The dots on the charts represent Kreis' confirmatory percentages.

This group of "partially dry" labors lends itself to analysis of the rôle of the amniotic sac. If the hydrostatic wedge concept is correct, then the earlier the membranes rupture the longer the labor should be; that is, there should be a high *negative* correlation between the relative

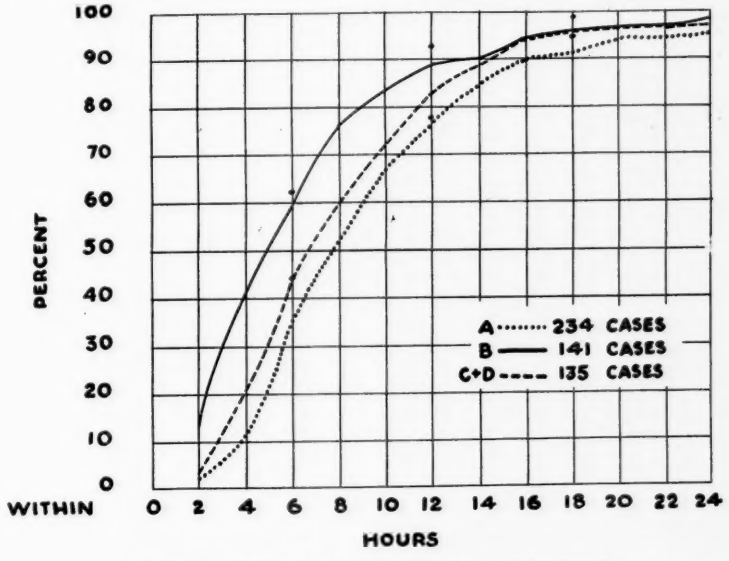

Fig. 2.—Ogive of labors completed, multiparas.

length of the "wet" portion of the labor and the total length of labor. The correlation may be worked out by plotting the total length of labor against the percentage of wet labor in each of the cases. Far from a high negative correlation in the 134 primiparas and the 130 multiparas so studied, there was a distinct and significant, even though small, *positive* correlation (0.20 ± 0.05 and 0.21 ± 0.05), that is, suggesting that the earlier the membranes ruptured the shorter the labor tended to be.

The simplest way of expressing the difference between so-called normal labor and dry labor and partially dry labor is by the averages of the lengths of labor. This is shown in Fig. 3. The control cases averaged 12.3 hours for primiparas; the partial dry group, 11.9 hours; and the dry labors, 10.3 hours. For multiparas the values were 8.5, 7.9, and 6.1 hours, respectively. The probable error of the mean in each case was

in the neighborhood of fifteen minutes.* These figures represent only labors terminating within twenty-four hours. Had the others been added the differences would have been even greater because of the larger number of prolonged labors in the "wet" group.

These results thus statistically confirm the conclusions of other writers on the subject, whose findings are presented in Fig. 4. Evidence that precocious rupture of the membranes leads to a higher percentage of prolonged labors or delays dilatation of the cervix and delivery, is conspicuous by its absence.

It will be remembered that when the hydrostatic wedge theory was first attacked, as early as the eighteenth century, preservation of the membranes was urged for other reasons, such as protection of the baby, and in later years the prevention of infection and cervical lacerations.

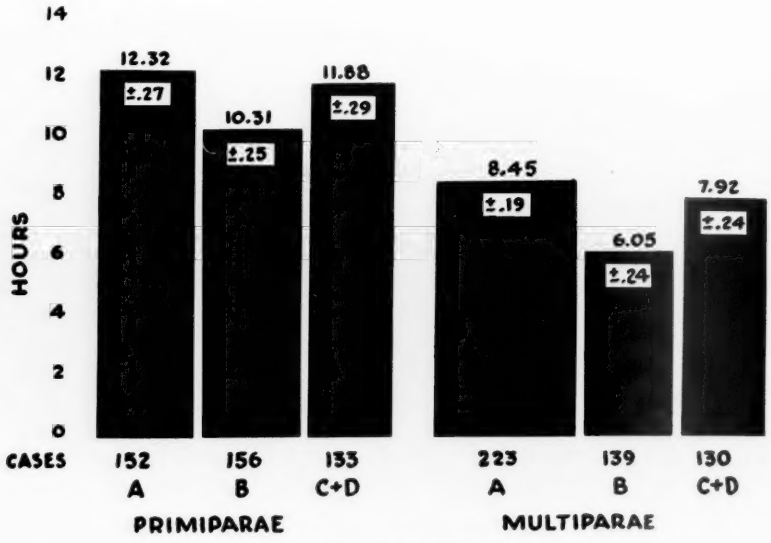

Fig. 3.—Average length of labor.

Again it must be pointed out that these are purely theoretical considerations. As W. D. Porter[16] commented in 1923: "The dangers of dry labor are rather exaggerated . . . and the dangers mentioned do not develop as a rule." One of these dangers is the increased incidence of

*The values were derived by the Pearson Product-Moment Coefficient technic from the formula:

$$r = \frac{\Sigma x'y' - \frac{(\Sigma fdx)\ (\Sigma fdy)}{N}}{\sqrt{\left(\Sigma fd^2x - \frac{(\Sigma fdx)^2}{N}\right)\left(\Sigma fd^2y - \frac{(\Sigma fdy)^2}{N}\right)}} \pm \frac{0.6745\ (1-r^2)}{\sqrt{N}}$$

The P.E.M. was calculated from the formula: $0.6745 \times \frac{\sqrt{\Sigma fd^2}}{N}$ and the Reliability of the Difference from the formula: $\frac{\text{Diff}}{\sqrt{(\sigma M_1)^2 + (\sigma M_2)^2}}$. The values for the reliability of the difference between the control and the dry labor groups were 3.68 and 5.36 for primiparas and multiparas, respectively.

forceps application. In Table III are presented the figures in this series for indicated low, mid and high forceps, excluding the prophylactic use

TABLE III. INCIDENCE OF FORCEPS INTERVENTION

	LOW, MID, HIGH FORCEPS	MID AND HIGH FORCEPS
A	16.3%	6.2%
B	10.6%	3.5%
C, D	12.6%	4.2%

of outlet forceps. The highest incidence was found in the control group, the lowest in the dry labor group, with the partially dry labor cases again falling between. Since the indications for forceps are usually maternal exhaustion or fetal distress, and since the incidence varies as the length of labor in the three groups, it is suggested that the lowered incidence in the dry and partially dry labors is due to their being shorter with the concomitant saving of energy to the mother and trauma to the child.

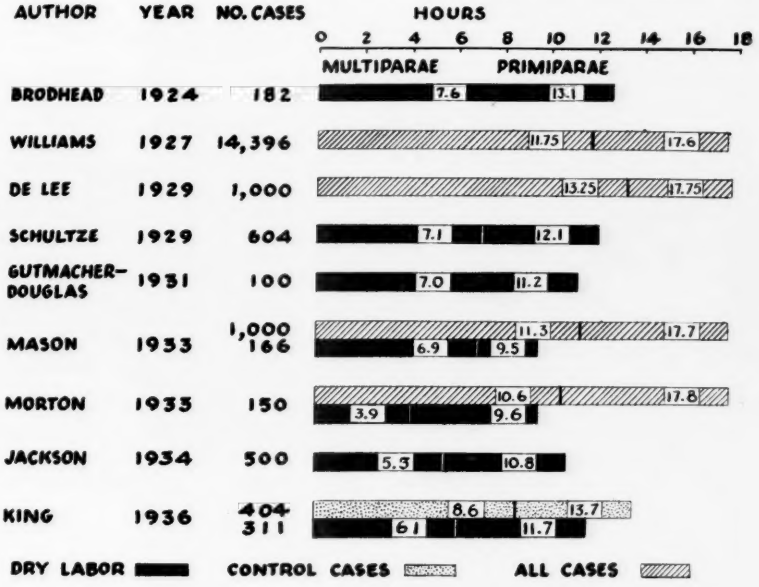

Fig. 4.—Average duration of labor.

Another of these dangers is that of infection. The morbidity in the 1,001 cases is given in Table IV. The standard used was that of the American College of Surgeons, a temperature of 100.4° F. on two successive days not including the first or later than the tenth day postpartum. It will be observed that the total morbidity was not appreciably raised and the morbidity from uterine causes was slightly lowered by premature rupture of the membranes. In this connection it is of some interest that Kreis first questioned the value of the membranes at the International Congress on Puerperal Fever at Strasbourg in 1922.[18]

From Denman's textbook[3] in 1778 to Curtis'[19] in 1933, the hydrostatic wedge has been considered gentle in its action on the maternal cervix. Norman Williams,[20] however, after a study of 150 cases in 1935, concluded that "the degree of dilatation at the time of rupture appears to bear a definite relationship to cervical injury . . . the tearing is found to be less when the membranes break before labor or early in labor." As shown in Table V this statement is to a certain extent confirmed in the 183 ward primiparas on whom postpartal data were available. From the limited number of cases no definite conclusions may be drawn, but it is apparent that intact membranes did not appreciably protect the cervix.

TABLE IV. MORBIDITY (A. C. S.)

	TOTAL	CORRECTED
A	6.2%	2.7%
B	5.5%	2.6%
C, D	6.6%	1.0%
D	6.7%	1.1%

TABLE V. CERVICAL LACERATIONS

183 PRIMIPARAS

	NO. CASES	0*	0 AND FIRST DEGREE	SECOND DEGREE	THIRD DEGREE
A	55	20%	80%	20%	0
B	68	30%	87%	12%	1%
C, D	60	17%	84%	18%	0

*No lacerations.

A very old argument in favor of preserving the membranes is the protection of the child. This is hard to discuss because of the complexity of factors and an endless amount of theorizing in the literature. As there was no death in the 1,001 normal cases that might have been attributed to the delivery, all the neonatal deaths and the viable stillbirths in the 1,621 admissions are presented in Table VI. It will be noted that there is no evidence to suggest dry or partially dry labors without complication were harmful to the child.

Since the results of this experiment were so contrary to the usual teaching, it was felt advisable to compare them with the observations on dry labor of the past fifteen years. There are abstracted in Table VII the opinions of all authors who have actually recorded their findings. It will be noted that there is a preponderance of evidence that dry labor, whether spontaneous or induced, is either harmless or even favorable, and the length of labor is unanimously conceded to be no more prolonged as a result of rupture of the amniotic sac, thus casting grave doubts on the rôle that structure plays in cervical dilatation.

TABLE VI. VIABLE STILLBIRTHS AND TWENTY-FOUR-HOUR NEONATAL DEATHS 1,621 OBSTETRIC ADMISSIONS

			?	A	B	C, D
Dead before onset of labor		14				
Anencephaly, meningocele, etc., prematurity		4				
Intracranial hemorrhage		0				
True knot in cord				1		
Cord tight about neck:	Accidental hemorrhage		1			
	Difficult breech				2	
	Difficult forceps			2	1	1
Prolapsed Cord:	Transverse or breech presentation				1	1
	During difficult version or high forceps			1	1	
	After bagging				1	
	In hydramnios			1		
Undetermined	Breech				1	
	Vertex		1	1		
Total vertex			2	6	3	1
Total	(36)	18	2	6	7	2

TABLE VII. SUMMARIZED OPINIONS ON DRY LABOR

AUTHOR	YEAR	NO. CASES	LENGTH LABOR	FORCEPS	MORBIDITY	FETAL DANGER	PROGNOSIS
Dorman, Lyon[21]	1921	270	Shorter	—	? Higher	? More	Same
Polak[17]	1923	—	—	—	—	—	Poor
Brodhead[22]	1924	182	Shorter	Same	Same	Same	Same
Randall[23]	1925	88	Same	—	—	—	Same
Schultze[13]	1929	604	Shorter	More	Higher	Less	Same
Norris[24]	1930	196	Shorter	More	Higher	Less	Poor
LaHaye[27]	1931	1250	Shorter	Fewer	Lower	Same	Good
Kreis[15]	1931	—	—	—	—	—	Good
Fitzgibbon[25]	1931	220	Shorter	Same	Lower	Same	Good
Gutmacher[26]	1930	761	Shorter	Fewer	Lower	Same	Good
Slemmons[28]	1932	132	Shorter	—	Same	Same	Same
Mason[14]	1933	166	Shorter	—	Lower	Less	Same
Morton[29]	1933	150	Shorter	—	Same	? Less	Same
van Rooy[30]	1933	—	—	More	—	—	Poor
Jackson[31]	1934	500	Shorter	? Fewer	—	Same	Good
A. G. King[10]	1934	300	Shorter	Fewer	Lower	Same	Good
E. L. King[32]	1934	—	—	—	—	—	Same
Woods[33]	1934	750	Same	? More	? Higher	Same	Same
Stern[34]	1934	85	Shorter	—	Lower	Less	Good
Holmes[35]	1934	90	Shorter	Same	Same	Same	Same
Rucker[36]	1935	716	Shorter	—	Lower	Same	Good
Krahulick[37]	1935	205	Shorter	—	—	—	Same
N. Williams[20]	1935	150	Shorter	—	Same	Same	Good
A. G. King	1936	597	Shorter	Fewer	Lower	Same	Good

SUMMARY

An investigation was made of 1,001 uncomplicated full-term parturitions occurring in 1,621 obstetric admissions. Of these, 40 per cent enjoyed intact membranes until complete dilatation and were used as controls. Thirty-one per cent spontaneously ruptured the membranes before the onset of regular pains at twenty-minute intervals, and were classed as dry labors. The remaining 29 per cent was made up of those whose membranes were intact only to a dilatation of from 4 to 7 cm., 11 per cent by spontaneous rupture and 18 per cent by deliberate rupture.

No light was thrown on the etiology of rupture of the membranes, although it occurred disproportionately more often in primiparas. Occipitoposterior position was not a factor.

The length of labor was studied from four points of view: There was a larger percentage of prolonged labors in the control group than in the dry and partially dry groups. The cumulative distribution curves of percentage completed labors at two-hour intervals, was most favorable for completely dry labors, least favorable for the "wet" labors, the partially dry labors falling between. In the partially dry labors there was a positive rather than a negative correlation between the length of the "wet" portion of the labor and the total length of labor. The statistically significant averages of the length of labor showed dry labor to be shorter than the controls by 2.0 (±0.25) hours for primiparas and 2.4 (±0.24) hours in multiparas.

Concerning the safety of labor in the absence of the membranes: The incidence of forceps intervention was 16.3 per cent in the control group, 10.6 per cent in the dry labor group, and 12.6 per cent in the partially dry labor group. The morbidity was essentially the same in all groups, i.e., 6.2 per cent in the controls, 5.5 per cent in the dry labor cases, and 6.7 per cent in the partially dry labors. There was a slightly lower incidence of cervical lacerations in the dry labor group than in the controls, with the partially dry labors falling between. The fetal mortality was unaffected by rupture of the membranes either spontaneously or deliberately.

The literature was exhaustively reviewed and reports in the last fifteen years amply confirm the above findings.

These results offer support to the explanation of cervical dilatation suggested by Dewees, that in labor the cervix is gradually retracted over the head by muscular action alone. On the other hand, that dilatation is accomplished by the hydrostatic wedge, a theory which has been disputed repeatedly since the eighteenth century, appears to be incompatible with the results of this experiment, inasmuch as the membranes proved to be unnecessary for a safe, easy, and short labor.

REFERENCES

(1) *Jacquemier, J.:* Manuel des Accouchements, Paris, 1846. (2) *Cazeaux, P.:* Midwifery, Am. ed. 3, from Fr. ed. 6, New York, 1863. (3) *Denman, Thos.:* Midwifery, London, 1805, p. 236 et seq., p. 349 et seq. (4) *Smellie, Wm.:* Midwifery, London, 1752, p. 204 et seq. (5) *Baudelocque, M.:* L'Art des Accouchements, Paris, 1789, Prgrph. 436. (6) *Burns, John:* Principles of Midwifery, ed. 6, London, 1824. (7) *Dewees, William Potts:* Compendious System of Midwifery, Philadelphia, ed. 1, 1826, ed. 6, 1833, p. 180 et seq. (8) *Sinclair, E. B., and Johnston:* Practical Midwifery, London, 1858, p. 24. (9) *Kreis, J.:* Gynec. et obst. **17:** 421, 1928. (10) *King, A. G.:* AM. J. OBST. & GYNEC. **27:** 576, 1934. (11) Personal Communication, June 5, 1935. (12) *Williams, J. W.:* Obstetrics, ed. 5, New York, 1927, D. Appleton-Century Co., p. 756. (13) *Schultze, M.:* AM. J. OBST. & GYNEC. **17:** 20, 1929. (14) *Mason, L. W.:* AM. J. OBST. & GYNEC. **26:** 394, 1933. (15) *Kreis, J.:* Gynec. et obst. **24:** 21, 1931. (16) *Porter, W. D.:* Discussion on paper by Polak,[17] AM. J. OBST. & GYNEC. **5:** 552, 1923. (17) *Polak, J. O.:* AM. J. OBST.

& GYNEC. **5**: 488, 1923. (18) *Kreis, J.:* Gynéc. et obst. **8**: 1923. (19) *Curtis, A. H.:* Obstetrics and Gynecology, Philadelphia, 1933, W. B. Saunders Co., p. 751. (20) *Williams, N.:* West. J. Surg. Gynec. Obst. **43**: 216, 1935. (21) *Dorman, F. A., and Lyon, E. C.:* AM. J. OBST. & GYNEC. **1**: 595, 1921. (22) *Brodhead, G. L.:* New York J. M. **24**: 801, 1924. (23) *Randall, L. M.:* Minnesota Med. **8**: 525, 1925. (24) *Norris, C. C.:* AM. J. OBST. & GYNEC. **19**: 500, 1930. (25) *Fitzgibbon, G.:* J. Obst. & Gynec., Brit. Emp. **38**: 495, 1931. (26) *Gutmacher, A. F., and Douglas, R. G.:* AM. J. OBST. & GYNEC. **21**: 485, 1931. (27) *LaHaye, P.:* Rev. franç. de gynéc. et d'obst. **25**: 657, 1930. (28) *Slemmons, J. M.:* AM. J. OBST. & GYNEC. **23**: 494, 1932. (29) *Morton, D. G.:* AM. J. OBST. & GYNEC. **26**: 323, 1933. (30) *van Rooy, A. H. M. J.:* J. Obst. & Gynec. Brit. Emp. **40**: 850, 1933. (31) *Jackson, D. L.:* AM. J. OBST. & GYNEC. **27**: 329, 1934. (32) *King, E. L.:* AM. J. OBST. & GYNEC. **28**: 763, 1934. (33) *Woods, E. B.:* J. Iowa State Med. Soc. **24**: 571, 1934. (34) *Stern, S. M.:* AM. J. OBST. & GYNEC. **27**: 701, 1934. (35) *Holmes, O. M.:* California & West. M. J. **41**: 241, 1934. (36) *Rucker, M. P.:* West Virginia M. J. **31**: 545, 1935. (37) *Krahulick, E. J.:* West. J. Surg. Gynec. Obst. **43**: 162, 1935.

3236 BURNET AVENUE

A SURVEY OF THE VAGINAL FLORA AT VARIOUS AGES, WITH SPECIAL REFERENCE TO THE DÖDERLEIN BACILLUS

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THE organism first discovered and described by Döderlein in 1892 has attracted the attention alike of bacteriologists, gynecologists, and obstetricians. Many students of bacteriology have been interested in this organism on account of its close relationship to the well-known intestinal type of lactobacillus, *L. acidophilus*. To the clinical group it is of particular interest because of the important rôle ascribed to it heretofore in the production of acidity of the vaginal tract. This acidity was and still is regarded by many as of prime importance in preventing infection of the genital organs, especially during pregnancy.

A number of investigators have made surveys of the prevalence of Döderlein's bacillus in the vaginas of individuals in various age groups. Much of their work has been done by the use of smear technics and cultural methods which appear to us to be inadequate for demonstrating the presence of the organism. In the work presented here we attempted to determine the frequency of occurrence of this bacillus in the vaginal tracts of children of various ages, pregnant and nonpregnant females, and in individuals infected with *N. gonorrheae*, using a culture medium which our experience has shown to be particularly favorable for the demonstration of members of the lactobacillus group. It was further desired to determine, if possible, from the data obtained, whether the Döderlein bacillus alone is responsible for the acid condition of the vagina, or whether the growth of the organism is merely a result of increase in H-ion concentration due to other factors. An

attempt was made also to determine what influence may be exerted by pathologic processes in the vaginal tract upon the presence or absence of the aciduric organism concerned here.

EXPERIMENTAL

In obtaining vaginal specimens for smear and culture, utmost precaution was taken to maintain as nearly aseptic conditions as possible. In infants and very young children the vulva was swabbed with tincture of green soap and dried with sterile towels. The labia were held apart with a gloved hand and a sterile swab inserted and drawn along the vaginal walls to absorb secretion; immediately, upon withdrawal, the swabs were immersed in a test tube containing 1 c.c. of sterile physiologic saline solution. A second swab was obtained in the same manner, for direct microscopic examination. In older children it was found impractical to use the green soap cleansing procedure because the groups, coming from charity camps, were too large to admit of this treatment. In these cases, with the labia spread as far apart as possible, it was relatively simple to insert the sterile swab through the opening of the hymen without contamination by contact with the vulva or anal region. Wherever contamination was at all suspected the swab was discarded. In pregnant and nonpregnant adults the specimens were obtained by inserting sterile vaginal specula and introducing the swabs directly into the vaginal vault. Adults with intact hymens were not included in this study.

All of the specimens were cultured within two or three hours after being taken. The swab was well rotated until the saline solution became cloudy. From one-half to three-fourths of this suspension was then plated in a medium having the following composition.

200 c.c. filtered tomato juice
5 gm. Difco peptone
10 gm. Difco peptonized milk
5 gm. Difco yeast extract
800 c.c. water
20 gm. Difco agar
pH adjusted to 7.5 sterilized at 180° C. for 8 minutes
Final pH near 6.6 to 6.7

The plates were incubated at 37° C. for forty-eight hours in an atmosphere containing 10 per cent carbon dioxide. They were then examined for the typical fuzzy colonies. Microscopic examination of a number of colonies, smooth and fuzzy, was always made in order to determine whether any of the smooth colonies contained the Döderlein organism. In no instance was this organism found to grow in any form other than that of the X or XY types. Reports of other observers to the effect that this organism may grow as a smooth colony may have been due to the use of media which particularly encourage this type of colony. The medium used in the work reported here has been found especially effective in accentuating the roughness of certain other members of the lactobacillus genus, namely *L. acidophilus* and *L. bifidus*. Further, unless pour plates are used, even on the medium described above, the organisms tend to grow in a smooth colony. It has always been observed by us that strains of the Döderlein bacillus which grow as the X or XY type of colony in a pour plate will be smooth in form when streaked on agar. Counts were made of the Döderlein colonies and those of all other bacteria appearing in the plate, and the results recorded in terms of percentage of Döderlein bacilli as compared with the total viable vaginal flora.

All of the smears were stained by Gram's method and the relative prevalence of aciduric rods, diphtheroids, gram-negative rods, and gram-positive cocci determined. A search was always made for gram-negative diplococci, and a hanging drop preparation examined for *Trichomonas vaginalis* in cases where a vaginal discharge was present.

RESULTS

A. *Children.*—The vaginal flora of 164 children was studied. The Döderlein bacillus was found to be present in 29 (17.7 per cent) of these individuals.

On further subdivision into the various age groups ranging from one to thirteen years, it was observed that of the children who were seven and one-half hours to six years of age (28 cases), 4 cases (14.3 per cent) showed the Döderlein bacillus. Of the children in the group aged seven years through twelve years (134 in number), 24 (17.9 per cent) harbored this vaginal organism. Only 2 individuals who were

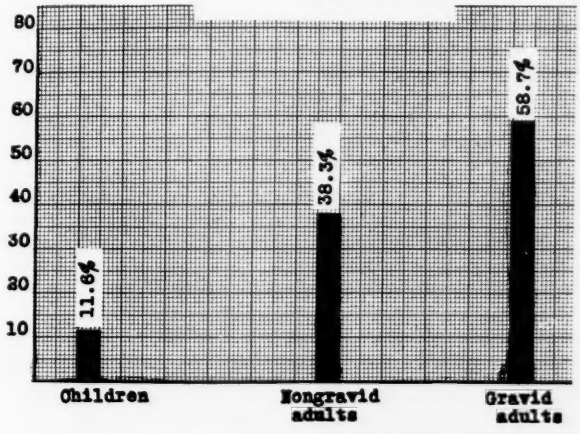

Chart 1.—Prevalence of the Döderlein bacillus in various age groups.

thirteen years old were studied, and of these only one had the Döderlein bacillus. Seven of the total number of cases studied had a vaginal discharge which could not be traced to gonorrheal or trichomonas infestation. Only 1 of these 7 patients harbored the aciduric bacillus.

B. *Nongravid Adults.*—Ninety-nine nongravid adult females were studied. Of these, 38 (38.3 per cent) showed the presence of the Döderlein bacillus, while 61 (61.7 per cent) had none. Further subdivision of this group into those complaining of vaginal disturbances (vaginal discharges or cervical lesions) and those having normal vaginal tracts, revealed that in the former group (45 in number), 17 (37.7 per cent) had Döderlein bacilli, and 28 (62.3 per cent) were apparently free from lactobacilli. In the latter group (54 in number), 21 (38.8 per cent) harbored the Döderlein bacillus, while 33 (61.2 per cent) did not. Of the group (45 in number) having vaginal disturbances, 10 of the 17 individuals who carried the Döderlein organism

suffered from a vaginal discharge, while 7 showed no discharge. Of those not harboring this vaginal bacillus (28 in number), 19 showed a discharge, and 9 did not.

C. *Gravid Females.*—A group of 97 pregnant women was studied. Of these, 57 (58.7 per cent) carried the Döderlein bacillus in the vaginal tract, while in 40 (41.3 per cent) the organism could not be demonstrated.

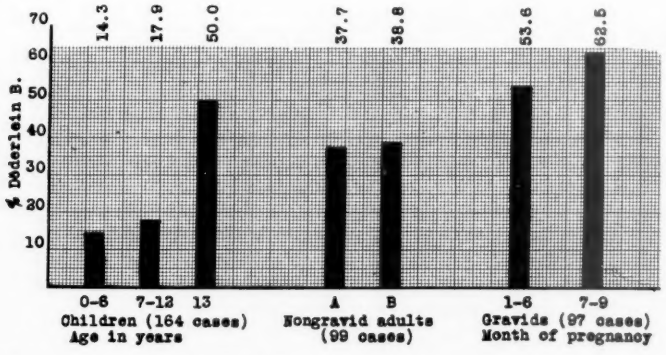

Chart 2.—In group of children, 7 showed vaginal discharge with no specific etiology; 1 showed Döderlein bacillus. *A*, Vaginal discharge or cervical lesion; *B*, normal vaginal tract. Group A, Döderlein bacillus present, 10 vaginal discharge and 7 no discharge; Döderlein bacillus absent, 19 vaginal discharge and 9 no discharge.

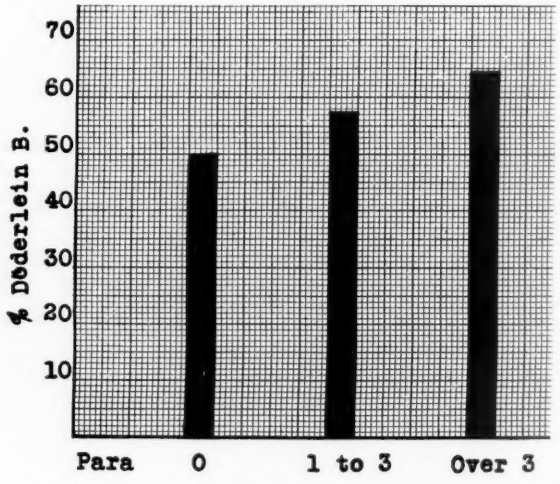

Chart 3.—Relation of Döderlein bacilli to number of pregnancies.

When the total group was analyzed from the standpoint of the month of pregnancy in which the vaginal examination was made, it was found that in the cases which were gravid from one to six months (41 in number), 22 (53.6 per cent) showed Döderleins, while 19 (46.4 per cent) did not. Of those who were pregnant from seven to nine months (56 in number), 35 (62.5 per cent had Döderlein bacilli, and 21 (37.5 per cent) did not.

Further subdivision of the group of gravid females, according to the number of children which they had borne, revealed that of those who had had no children (6 in number), 3 harbored Döderleins. Among women who had given birth to from 1 to 3 children (54 in number), 31 (57.4 per cent) showed this organism, while in 23 (42.6 per cent), it could not be found. Of 37 women who had more than 3 children (4 to 11), 24 (64.7 per cent) harbored Döderleins, while 13 (35.2 per cent) showed none.

Twelve individuals of the entire group of 97 studied had a vaginal discharge which was not due to gonococcus or trichomonas infection. In only 5 (41.6 per cent) of these was the presence of the Döderlein bacillus demonstrable.

D. *Specific Infection of the Vagina.*—Forty-two patients having specific vaginal infection were studied. Of these, 35 were found to harbor *N. gonorrheae,* while 7 were infected with *Trichomonas vaginalis.* It is of interest to note that none of these cases, the diagnosis of which was confirmed in every instance by stained smears, hanging drops and cultures, showed the Döderlein organism.

DISCUSSION

It should be noted in the results presented here that certain groupings of subjects have been made according to age in children, duration of pregnancy, and number of children in the pregnant groups. This grouping is purely arbitrary, and was decided upon for the purpose of working with significantly large groups.

Studies of the vaginal flora of 164 children revealed that 17.7 per cent harbored the Döderlein bacillus in their vaginal tracts. This figure is higher than that reported by Thomas[5] in 1928, who, working with a smaller group, reported a 10 per cent occurrence of Döderleins. It is of interest to note that, with the exception of two cases (thirteen years of age), none of the children studied had menstruated. It is significant that of those who were in the age group of seven through twelve years (134 in number), only 17.9 per cent harbored Döderleins. None of these children had menstruated, but a large number of them showed beginning or marked secondary sexual characteristics. On the other hand, the children ranging in age from seven and one-half hours through six years, none of whom showed any of the sexual changes observed in the former group, exhibited almost the same prevalence of Döderlein bacilli (14.3 per cent). It is regrettable that only two children who had menstruated were available for study and that consequently no conclusions could be drawn from this group. However, in our study of nongravid adults the effect of menstruation was determined, since no nonmenstruating individual was studied.

An inspection of the results obtained in the examination of the vaginal flora of 99 nongravid adults reveals that 38.3 per cent harbored Döderlein's bacillus. There seemed to be no correlation between vaginal pathology and the presence or absence of the Döderlein organism, since in the group of women showing vaginal pathology, 37.7 per cent harbored Döderleins, while in the group revealing no pathology 38.8 per cent showed Döderleins.

The data obtained in the group of gravid females analyzed from the standpoint of duration of pregnancy show that a higher percentage of women pregnant from seven to nine months (62.5 per cent) harbored the Döderlein bacillus than did those of the group of individuals gravid from one to six months (53.6 per cent). Since the number of individuals in each of these groups is approximately the same, some significance may be attached to the difference noted. This will be discussed later. No correlation could be drawn between the parity of the individual and the presence or absence of the Döderlein organism. Twelve of the group of gravid individuals studied showed a vaginal discharge. The occurrence of Döderleins in this group was somewhat lower (41.6 per cent) than that of the group as a whole.

Many investigators have shown that the Döderlein organism is absent when gonorrheal infection is existent. Most of this work has been done by using the smear method for detection of the aciduric as well as the gram-negative diplococcic forms. In the present study these results have been confirmed by cultural examinations. Although the number of cases of trichomonas infection studied is quite small, it is interesting to note that the vaginal lactobacillus was not found in any of such cases. Further work along this line is desirable.

Attempts to correlate the findings in the smears with those obtained in culture were not successful in many instances. Very frequently organisms resembling the Döderlein bacillus were observed in the slide preparations, but could not be found by the culture method. The converse was also frequently true. This fact, we believe, is illustrative of the difficulty involved in attempting to study the prevalence of this organism by the use of smears only. It was noticed that in some of the slides where the aciduric organism preponderated, the diphtheroid and gram-negative forms were the first to disappear, and the group of gram-positive cocci the last. In other words, three types of flora could be observed, according to the smear picture. First, a pure or almost pure specimen of Döderlein's organism; second, the aciduric rods mixed with gram-positive cocci; and third, the aciduric rods, gram-positive cocci and diphtheroid cells. Gram-negative rods were seen only infrequently and then only in the third group. The three types of vaginal flora observed by us have been described previously by Cruickshank[1] (1930) and others.

The question of association of Döderlein's bacillus with increased H-ion concentration in the vagina has interested many observers. We believe that no evidence exists at the moment which is in full support of the theory that the organism alone causes the increased acidity. Analysis of the above data indicates that there is a gradual increase in prevalence of Döderlein's organism in children up to puberty, that the organism is to be found much more frequently in nongravid adults, and that it reaches its highest frequency level in the gravid adults in the last two or three months of pregnancy. It is a known fact that the vaginal H-ion concentration is lowest in children, higher in nongravid females, and highest in the pregnant females, especially in the last two or three months of gestation. It is also recognized that estrin is present in small quantities in prepubertal children, increases in amount as the menstrual function becames established, and reaches its highest concentration during pregnancy and especially in the last two or three months. It has been shown by Hall and Lewis[3] in monkeys (1936) and by Lewis and Weinstein[4] in children, that the administration of estrin increases vaginal acidity, and that in some cases where Döderlein's bacillus was not present before administration of estrin, it was present after this treatment. Since the Döderlein organism is known to be favored by an acid medium, and the other members of the vaginal flora, such as the gram-negative rods, diphtheroids and gram-positive cocci are inhibited by a low pH, it seems probable that the presence of the vaginal bacillus is the result in many cases of the acid reaction brought about in the vagina by such factors as the natural or artificial introduction of estrin. The vaginal acidity does not seem to be due merely to the presence of the Döderlein organism, but it seems likely that the presence of the aciduric bacillus is facilitated by the increased acidity, which in turn is brought about by secretion of estrin.

CONCLUSIONS

1. A survey of the vaginal flora of 400 females of various ages revealed that 17.7 per cent of children, 38.3 per cent of nongravid females, and 58.7 per cent of pregnant women harbored Döderlein's bacillus.

2. There seemed to be only a slightly increased prevalence of the Döderlein organism with increase in age in the prepubertal group.

3. Döderlein's bacillus was found more frequently in the later than in the earlier months of pregnancy, and in the group of women who had borne 3 to 6 children, as contrasted with those who had given birth to 1 to 3 children.

4. Very little correlation could be drawn between vaginal pathology and the absence or presence of the aciduric vaginal bacillus, except in cases of gonococcus or trichomonas infection, in which Döderlein's organism was never demonstrated.

5. Three types of vaginal flora, as observed by other investigators, were noted in the direct microscopic studies.

6. Some evidence is presented in support of a theory that the presence of Döderlein's bacillus in the vagina is the result of the acidity induced by the secretion of estrin, and that the organism itself is not responsible for vaginal acidity.

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REFERENCES

(1) *Cruickshank, R., and Baird, D.:* Edinburgh M. J. **37:** 135, 1930. (2) *Döderlein, A.:* Verhandl. d. deutsch. Gesellsch. f. Gynäk. p. 35, 1892. (3) *Hall, and Lewis, R. M.:* To be published in Endocrinology. (4) *Lewis, R. M., and Weinstein, L.:* To be published in Surg. Gynec. Obst. (5) *Thomas, S.:* J. Infect. Dis. **43:** 218, 1928.

THE LE FORT COLPOCLEISIS*

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SINCE 1931, 38 cases of partial or complete genital prolapse in older women have been treated at the Chicago Lying-In Hospital by some modification of the Le Fort colpocleisis. This operation consisting of a medial obliteration of the vagina is seldom performed. The operation is applicable to a difficult group of cases, and the results have been so satisfactory that it would seem to be of value to report the cases with the method of treatment, since colpocleisis is seldom used and the literature is small compared with the great bulk written on the general subject of genital prolapse and its treatment.

The history of the surgical treatment of prolapse and the development of the operation may be of interest. The first attempts at surgical remedy consisted in an amputation of the protruding parts or a reduction of the size of the introitus to prevent their downward displacement. Frick of Hamburg (1832) sutured together the lower third of the labia majora. Credé, Baker-Brown, Dieffenbach, and Scanzoni denuded the tissues around the introitus and sutured the parts. Others removed portions of the vaginal walls and apposed the raw surfaces. All of these operations were done after a reduction of the prolapse. None of them were very successful.

As early as 1823 Gérardin of Metz adopted cauterization of the vaginal walls as treatment, and he first suggested that the anterior and posterior portions of the

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vagina might be denuded at the introitus and the surfaces approximated by sutures. He did not perform the operation. It was first attempted by Neugebauer of Warsaw (1867). He denuded an area 3 by 6 cm. on the anterior and posterior walls near the introitus and sutured the anterior to the posterior wall at a somewhat higher level (3 cm.). His work was published in Polish journals (1867, 1870, 1871), but the method was not popularized until cases were reported by Léon Le Fort, Professor of Medicine, Paris, in 1876.

Le Fort knew nothing of the work of Neugebauer but followed the suggestion of Gérardin. He was led to use the colpocleisis as a result of his own work on congenital vaginal septum, the results of which he published in 1863. He observed that prolapse did not occur in cases of congenital septum of the vagina, and that, as a rule, normal sexual relations were possible and childbearing was not interfered with. Since treatment of prolapse was often necessary in women of childbearing age, a satisfactory operation must take these two factors into consideration.

Le Fort differed from his predecessors as to the cause of genital prolapse. He was of the opinion that in cases of genital prolapse, due to childbirth trauma or to congenitally poor tissue support, the hypertrophy and elongation of the cervix usually found, were secondary, not primary. He thought that the relaxation of the vaginal wall following childbirth, together with the usual rupture of the perineal floor, allowed a sinking downward of the anterior vaginal wall and the rectovaginal septum. The weight of the bladder upon the relaxed wall would result in a cystocele which would tend, in turn, to pull down after it the "next-lying vaginal wall." Traction would thus be put upon the cervix and in time lengthen both the supravaginal and infravaginal portions. The continuous, slight, downward traction would be responsible for the gradual prolapse of the corpus and its relaxed supports. He thought, therefore, that if it were possible to hold the vaginal walls in apposition and to prevent their sinking downward, it might be possible to prevent prolapse of the uterus.

His first patient, in 1876, was a twenty-nine-year-old woman, para iv, with a complete uterine prolapse, third-degree rectocele and cystocele. To the partial vaginal septum which he made, he added a perineal repair after the manner of Baker-Brown. The operation was successful. The following year the patient was delivered of a living eight-month fetus after a short, normal labor. The septum, of course, was incised. No recurrence of the original condition followed.

The technic of the operation as described by Le Fort is as follows:

"With the patient in the dorsal position and without attempting to replace the uterus, which was entirely outside the vulva, I made four incisions on the lower portion of the anterior wall of the vagina, circumscribing a strip of mucous membrane which, when removed, gave me a raw surface about 6 centimeters in length and 2 in breadth. Then, after raising and lifting the prolapsed uterus toward the abdomen, thus exposing the posterior surface of the tumor, I produced on this part a denuded surface similar to the one on the anterior wall. After doing this, I exposed the uterus sufficiently to permit joining the ends of the two raw surfaces which were closest to the uterus, and I applied sutures at three points on the transverse margin, uniting linearly the anterior and posterior walls of the vagina. I proceeded then to unite the lateral edges with a silver wire passed through corresponding points on the anterior and posterior margins of each side. A wire having been similarly placed at the same height on the opposite margin, the reduction of the uterus was increased by drawing together the apposed vaginal walls through a tightening of the two sutures. The reduction progressed step by step with the placing of the sutures, and when the two margins of the raw surfaces were united throughout, the reduction was complete." (Passage translated from original article by Léon Le Fort.)

In the years immediately following, numerous surgeons performed the operation, modifying the original technic. Eustache increased the width and depth of the vaginal septum, thus augmenting the stability of the uterine support and lessening the likelihood of recurrence of the prolapse through one of the lateral canals. This, however, interfered with coitus and reduced the applicability of the operation to women past the age of active sexual life. Duplay added a perineorrhaphy to the colpocleisis. After 1900 only occasional reports appeared in the literature until 1925. Since that time reports of small series of cases have been made by several operators (Brocq and Nora, Baer and Ries, Phaneuf, etc.). The history of the operation and the literature have been discussed at length because there is no such résumé in English and the material was found in old journals inaccessible to many practitioners.

In spite of the rarity of the performance of colpocleisis there would seem to be a place for such a procedure in a limited number of cases of prolapse. It is a relatively simple surgical procedure. It is admirably suited to elderly women and may be used when more extensive operations are contraindicated because of obesity, hypertension, chronic nephritis or evidence of myocardial weakness. In the cases reported here, 64 per cent had some condition contraindicating extensive operative procedure. It may be used with excellent results where other operative methods have failed. It can be carried out under local anesthesia or with a minimum of gas anesthesia or ethylene.

The prerequisites for the operation are as follows: The sexual life of the patient should no longer be of importance and the consent of the husband should be obtained. The cervix, corpus, and adnexa should be free from pathology. Schwabe thinks that all cases should be curetted prior to the operation and that phenol cauterization of the uterine cavity should be carried out. Erosions of the cervix and vaginitis should be eliminated by suitable treatment. The prolapse should be capable of reduction.

In the 38 cases presented here the ages of the patients vary from fifty-seven to seventy-three years (mean age = sixty-four years) and the duration of their complaint from one to forty-four years. One patient had never been pregnant; the rest had borne from 1 to 11 children. They were from four to twenty-eight years past the age of menopause. Nineteen (50 per cent) had had previous surgical treatment for the condition present. Eleven had worn various types of pessaries unsuccessfully.

The symptoms from which the patients suffered were chiefly urinary and pelvic. These included pollakiuria, dysuria, difficulty in urinating, retention of the urine with resulting cystitis and a sense of bladder

pressure. The discomfort of the prolapse and its interference with walking was a frequent complaint. Other symptoms were vaginal discharge and spotting, and in one case vulvitis.

On examination the pathology found was as follows: complete prolapse in 10 patients, complete prolapse with enterocele in 1, complete recurrent prolapse after hysterectomy in 4, partial prolapse with rectocele and cystocele in 18, and rectocele and cystocele alone in 5.

Surgical treatment was complicated by those conditions commonly found in elderly women—hypertension, obesity, albuminuria, and diabetes mellitus. The two cardiac patients were poor risks; another patient had been treated for pernicious anemia for some time.

Each case was given individual consideration in the choice of operation, and the colpocleisis was combined with other operative procedures as indicated by the pathology present. It was found that the addition of a perineorrhaphy added greatly to the results if a relaxed pelvic floor were present. A plication of the vesicovaginal fascia in cases with large cystocele also greatly improved the result of operation.

The operations performed were as follows:

Le Fort colpocleisis + plication of vesicovaginal fascia + perineorrhaphy	11 cases
Le Fort colpocleisis + perineorrhaphy	15 cases
Le Fort colpocleisis + repair of inguinal hernia	1 case
Le Fort colpocleisis + plication of vesicovaginal fascia + perineorrhaphy + repair of enterocele	1 case
Le Fort colpocleisis + vaginal hysterectomy	5 cases
Le Fort colpocleisis	5 cases

The operations were not all carried out by a single operator, but in general the technic consisted of three procedures:

1. Plication of the pubovesical fascia.
2. Le Fort colpocleisis.
3. Colpo-perineorrhaphy.

THE TECHNIC OF LE FORT COLPOCLEISIS

The patient is placed in the lithotomy position and the usual perineal and vaginal preparations, catheterization and draping completed. Either local anesthesia (½ of 1 per cent solution of novocaine) or light ethylene anesthesia is used. The cervix is grasped in the midline and drawn downward with a single-toothed tenaculum forceps.

The first step in the Le Fort colpocleisis is beginning the denudation of the anterior vaginal wall by a snowshoe-shaped incision of approximately 4 by 8 cm. The base of the incision is just above the bladder reflection. The vaginal flap is dissected free downward to the fascial layer and extended toward the urethra for a distance sufficient to expose the vesicovaginal fascia.

The bladder wall is exposed mesially close to the cervix and is pushed upward on the uterus. The fascia is split in the midline and is then sutured to the uterus underneath the bladder wall as in a cystocele operation.

The cervix is drawn forward and a similar flap of mucosa is freed posteriorly.

A transverse strip of vaginal mucosa about 2 cm. wide is thus left across each of the lips of the cervix. The margins of these anterior and posterior strips are sutured to one another with interrupted sutures, thus making a transverse channel below the level of the internal os. These interrupted sutures are inserted so that they enter and emerge on the vaginal surface and the knots, when tied, lie within the vaginal channels.

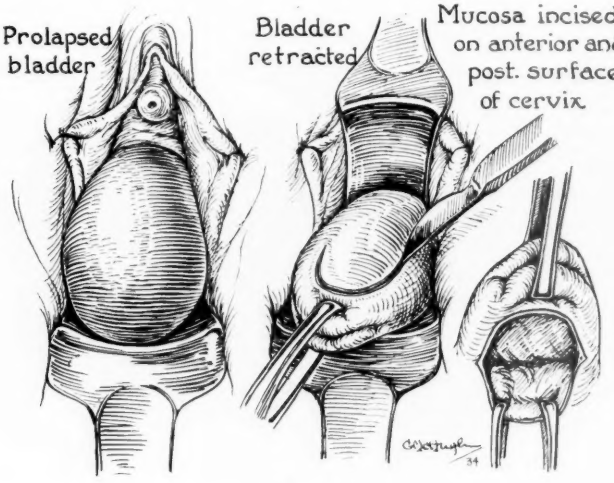

Fig. 1.

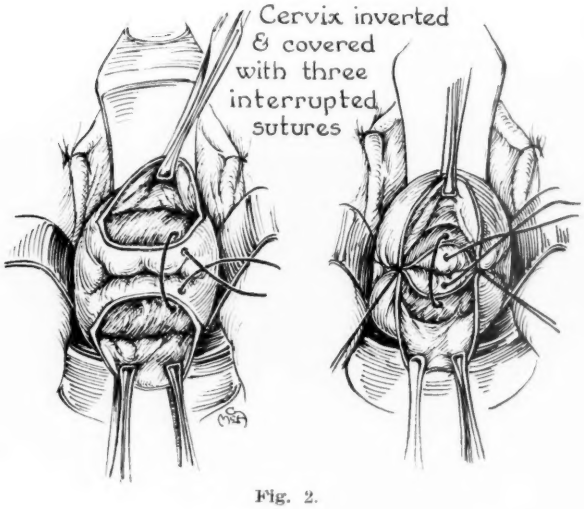

Fig. 2.

The lateral strips of vaginal mucosa are about 1.5 to 2 cm. wide, extending from the transverse cervical strip superiorly to a point about 1 to 1.5 cm. above the external urethral meatus and inferiorly to fuse with the perineorrhaphy incision.

The lateral margins of the vaginal mucosal flaps are sutured by interrupted sutures anteriorly and posteriorly. These sutures are inserted and tied with the knots inside the lateral channels as described above. As the margins are sutured

downward, the uterus recedes upward and gradually right and left channels about 0.5 cm. in diameter are formed which ultimately extend from the cervix downward to the introitus.

The operation is completed by a typical perineorrhaphy.

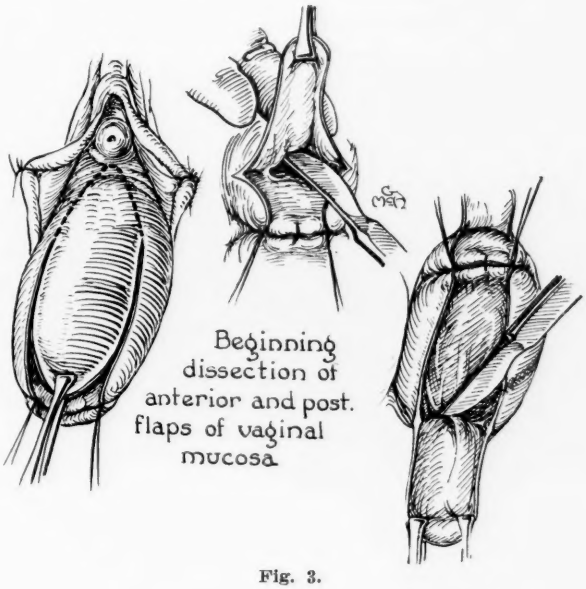

Fig. 3.

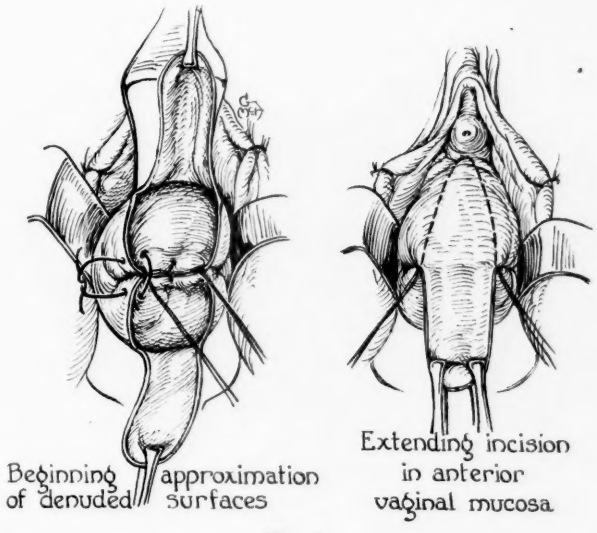

Fig. 4.

The lateral and transverse channels make an inverted U-shaped channel. The lateral channel of one side runs upward from the introitus to the cervix, passes across below the external os to connect with the lateral channel of the opposite side which extends downward to the introitus. The lateral channels can be easily demonstrated by the insertion of a uterine sound.

Convalescence.—The patient is usually awake before leaving the operating room. The light anesthesia required generally reduces postoperative nausea to a minimum. Patients are kept comfortable with small doses of morphine sulphate and placed on liquids and a light diet. They are encouraged to move about. Recovery is surprisingly rapid. The patients in seven of the cases here reported had mild febrile reactions. Three developed a postoperative cystitis, and two had a slight discharge from the operative area. Three patients had prolonged hospital stays of seventeen and nineteen days. The remainder were up and about on the ninth and tenth post-

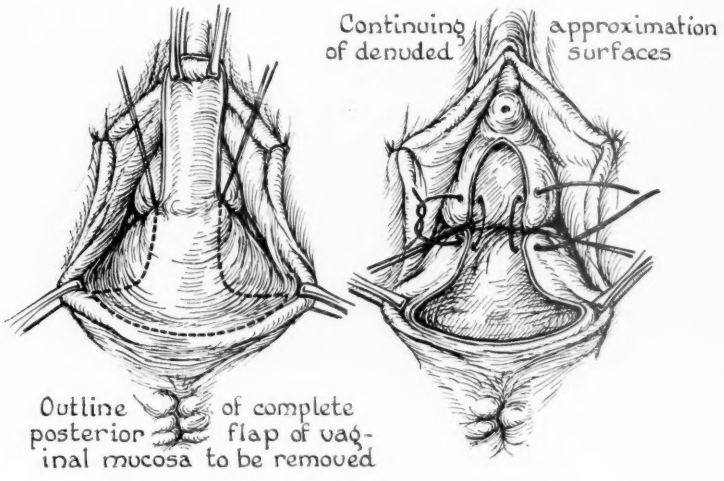

Fig. 5.

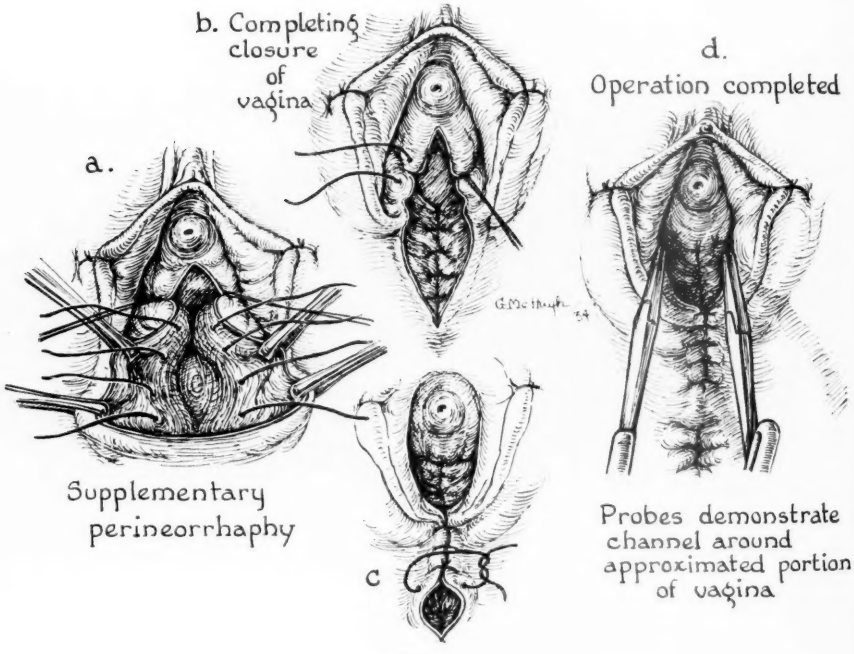

Fig. 6.

operative days and left the hospital on the twelfth or fourteenth postoperative day. There were two fatalities in the series, a mortality of 5.26 per cent. While the condition responsible for the first fatality was not directly connected with the operative procedure or a condition growing out of the event, it should be charged to the mortality since the patient died while in the hospital. The patient, aged fifty-eight years, had been considered a poor cardiac risk by the medical consultant; operation had been carried out under local infiltration anesthesia (novocaine ½ per cent). On the eighth postoperative day the patient developed a coronary thrombosis which was followed by auricular fibrillation. A popliteal embolism occurred with resulting gangrene of the left leg; and on the thirty-ninth postoperative day the patient died from hypostatic pneumonia. The second fatality was due to pulmonary embolism in a patient who had slight postoperative fever. The embolus occurred after the patient had been allowed up on her thirteenth postoperative day.

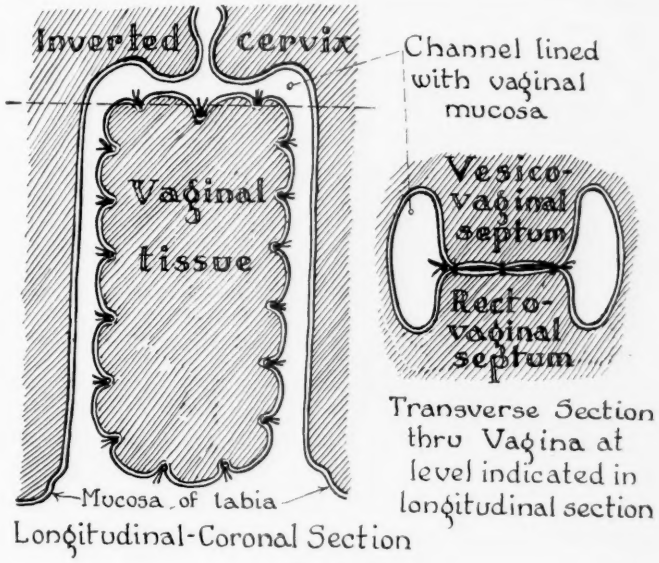

Fig. 7.

RESULTS

The results of the operation should not be finally appraised before the end of one year. In this series the follow-up of the survivors ranges from three months to over three years. To date there has been one recurrence. The uterus prolapsed through one of the lateral channels three months after operation. This was corrected by a secondary operation. In all of the other cases the functional results have thus far been excellent. In two of them the anatomic results were not entirely satisfactory. On inspection there was a very slight bulging anterior to the transverse line of suture. This slight cystocele might well have been due to failure to carry the denudation of the anterior vaginal wall low enough beneath the urethral meatus. In no case has there been failure of the surfaces to unite. Satisfactory final results were

thus obtained in 94.74 per cent of the cases in this series. This compares favorably with the results reported in the literature. In a total of 260 cases reported by various operators from 1867 to 1930, there was a satisfactory result in 86 per cent of the cases. It is of interest to note that the causes for recurrence of the prolapse have been almost universally the same: (1) Failure to make the lateral channel small enough to prevent recurrence of the prolapse through the side canal; and (2) failure of the sutures to hold, with resulting partial separation of approximated surfaces. Deaths have usually been due to thrombosis and cardiovascular disease.

There has been one major objection to the operation: the performance of colpocleisis precludes any further examination of the cervix. For this reason it is necessary that the cervix and the uterus should present no abnormality at the time of operation, and if any suspicious lesion is present, a vaginal hysterectomy should be done. However, the incidence of uterine carcinoma in women with atrophied uteri is indeed rare. We have found a report of only one case of carcinoma following colpocleisis.

REFERENCES

Baer, J. L., and Ries, R. A.: Am. J. Obst. & Gynec. **16**: 646, 1928. *Börjeson, Curt:* Acta obst. et gynec., Scandinav. **5**: 235, 1926. *Brocq, P., and Nora, G.:* Gynéc. et Obstét. **11**: 338, 1925. *Crossen, Harry Sturgeon:* Operative Gynecology, ed. 4, St. Louis, 1930, The C. V. Mosby Company. *Dubois, V.:* J. de méd. de chir. **2**: 48, 1889. *Eustache, G.:* Arch. de tocol. **9**: 513, 1882. *Le Fort, Léon:* Ann. de gynéc. et d'obst. **7**: 299, 1877. *Phaneuf, Louis E.:* Am. J. Obst. & Gynec. **30**: 544, 1935. *Rice, Annie E.:* Maryland M. J. **10**: 769, 1884. *Rubovits, William, and Litt, Sol:* Am. J. Obst. & Gynec. **29**: 222, 1935. *Schwabe, Lorenz:* Monatschr. f. Geburtsh. u. Gynäk. **44**: 396 and 468, 1916. (Extensive bibliography.) *Wyatt, James:* J. Obst. & Gynec., Brit. Emp. **22**: 266, 1912.

Brown, Dorothy: Double Pyosalpinx Due to Salmonella Newport Infection, Lancet **2**: 1173, 1935.

A married woman, aged twenty-six, who had never been pregnant began to suffer from backache and slight chilliness. She continued with her work. For days later her physician found a fever and lower abdominal tenderness. On the twenty-first day of the disease the patient was hospitalized with a temperature of 101.6° and pulse of 128. At operation a large left pyosalpinx and a smaller left pyosalpinx were drained. Cultures of the pus were made especially because the condition resembled tuberculosis. The convalescence was satisfactory. There was no evidence of diarrhea, constipation, nausea, etc.

By smear and cultural studies and agglutination and antigenic tests the organism was identified as Salmonella Newport. (This is a gram-negative bacillus and is a genus of the bacteriaceae.) Recovery of the organism from the blood, urine, and feces failed. The source of the infection could not be determined.

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ACUTE NEPHRITIS AND PREGNANCY*

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COMPARATIVELY few reports of acute nephritis or nephrosis and pregnancy have been published. These conditions either are rare or are overlooked in the diagnosis. "Toxemia of pregnancy" is an inclusive term for all cases of edema, albuminuria, or hypertension in pregnancy. Disease of the vascular-renal system may be caused by the toxemia itself, or it may be pre-existent to the pregnancy, in which event it is usually aggravated. Many toxemia patients have symptoms and signs of acute nephritis or nephrosis, but they usually disappear rapidly after delivery. The abnormal findings, which we will describe, were found to persist in a small group of these patients.

Acute nephritis, hemorrhagic Bright's disease, or acute glomerulonephritis may be defined as the occurrence in a previously normal patient of proteinuria, cylindruria and hematuria. Edema, hypertension, and oliguria may also be present. A retention of the blood nitrogen and generalized convulsions may occur. Occasionally there are pathologic changes in the retinae. The disease usually appears during convalescence from some streptococcal disease, such as tonsillitis or scarlet fever. The onset is occasionally so insidious that its origin cannot be determined. It is self-limited and complete recovery may occur in a period of several months to a year and a half. If the abnormal urinary findings are still present at the end of two years, the disease is then considered a chronic glomerulonephritis.

Acute nephrosis, lipoid nephrosis, degenerative Bright's disease or the nephrotic form of glomerulonephritis are the various terms used to describe cases without hypertension but with massive edema, marked proteinuria, slight, if any, cylindruria, and no hematuria. The characteristic findings in the blood are a decrease in the hemoglobin, a serum protein concentration of less than 5 per cent, an albumin: globulin ratio of 1 or less, a marked increase in cholesterol and total lipids, and little or no nitrogen retention. Doubly refractive lipoid bodies, both free and in the casts, are found in the urine. The loss of protein in the urine tends to be constant and ranges from 5 to 50 gm. per day. If the previously described symptoms occur in a child or young adult, it may be a case of true nephrosis, as described by Leiter, but, in general,

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it has been our experience that the majority of the cases seen by us are the atypical form of acute glomerulonephritis. This syndrome is often diagnosed "albuminuria of pregnancy."

The toxemias of pregnancy are characterized by vascular and renal pathology. The symptoms and signs may be present for a period of a few days or weeks or they may remain after delivery. The presence of albumin and casts indicates an abnormal condition of the kidneys and some investigators refer to such cases as the "nephrosis" or the "nephropathy of pregnancy." A patient with an acute toxemia of pregnancy, whether it is preeclampsia or eclampsia, may have blood in the urine on microscopic and macroscopic examination. In our experience, however, this abnormal increase in erythrocytes has been transient, disappearing within a few days. If the duration is longer and if there are other characteristic pathologic urinary findings, we believe that a diagnosis of acute nephritis is more likely to be correct. It seems obvious that if the same vascular spasm occurs in the kidney as is found in the vessels of the retinae and the brain, it may be the cause of albumin, casts and erythrocytes in the urine. These various conditions are described best by the following typical cases.

ILLUSTRATIVE CASES

Lipoid Nephrosis.—Patient 11, aged twenty-two years, was admitted to the hospital on Jan. 14, 1927, in her first pregnancy and at term on May 17, 1927. She had had an erysipelas of the face in May, 1926. Edema of the ankles was first noticed after she became pregnant. It gradually increased and dyspnea was noted during the past month. Marked pallor, general anasarca, a double hydrothorax, ascites, and a marked edema of the labia were noted on examination. The uterus was the size of an eighteen weeks' gestation. Ophthalmoscopic examination showed edema of the retina and disk of the right eye, and slight edema of the left retina. The blood Wassermann was negative. An x-ray diagnosis of bilateral maxillary sinusitis was made. The patient was discharged on Feb. 7, 1927. She was readmitted on February 27 and was delivered of a macerated fetus. After the delivery she became even more edematous and there was a marked oliguria. On March 18, examination of the eyes showed an optic atrophy of the right eye and questionable involvement of the left. She was discharged on March 30. On June 6, 1927, she again returned and was found to be eight weeks pregnant. An abdominal hysterotomy and sterilization were performed on June 18, 1927. The patient stated that she had repeatedly observed swelling of the extremities following the ingestion of fat, even in minimal amounts, while she was still seated at the table.

During hospitalization the patient was on a chloride-poor diet, which consisted of 150 gm. of protein, 150 gm. of fat, and 300 gm. of carbohydrate. The diet yielded 3,200 calories, but she never consumed over 2,500 calories and usually much less. A sufficient amount of protein was never consumed. The nitrogen intake over a sixty-five-day period ranged from 5 to 21 gm., with an average of 7.4 gm. per day. The average total nitrogen in the urine was 7.9 gm. per day. The protein in the urine ranged from 7 to 22 gm. per day. In a period of nineteen days she lost 14 kg. in weight. She did not cooperate well after delivery and was seen irregularly. From 1930 on there was little or no edema, but her blood pressure had started to increase. In 1934 there was a very definite anemia, for which she was given a blood transfusion. The patient died of uremia in December, 1934. No autopsy was

performed. The clinical course and termination, however, indicate that what at first appeared to be a lipoid nephrosis was, in all probability, a nephrotic type of glomerulonephritis (see Table I).

Acute Glomerulonephritis.—Patient 1, aged twenty years, was admitted to the hospital on Sept. 12, 1933, in her first pregnancy, and approximately seventeen weeks pregnant. She had always been well until the onset of edema of her feet and lower legs one month previously. At this time there was urinary frequency, burning on urination, nocturia, and the urine was dark. Examination showed a two-plus edema extending up to the knee and a blood pressure of 154/90. The patient was treated for one month, with no improvement and possibly some increase in the severity of the process, as indicated by the decrease in the clearance, the anemia, etc. A therapeutic abortion was performed on October 13. The subsequent course was that of a chronic glomerulonephritis. There was a persistent albuminuria, varying from 5 to 12 gm. per day, with casts and a slightly increased number of erythrocytes, according to the Addis technic. The patient has been on a salt-

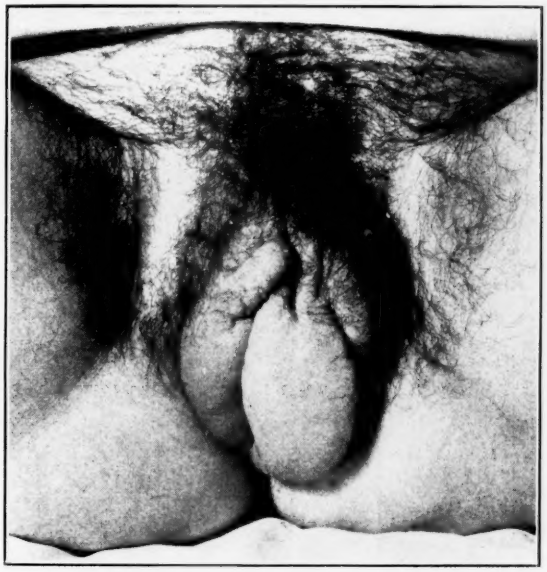

Fig. 1.—Patient 5. Nephrotic glomerulonephritis. Note marked swelling of vulva, which was present for one week.

poor general diet since her discharge from the hospital but the edema still persists. Because of the lowered serum protein and especially the lowered oncotic pressure of the serum she has been on a high protein diet for the past year. Her last blood pressure was 155/110. There is still a two-plus edema. On Dec. 17, 1935, she returned again and was found to be pregnant. A therapeutic abortion was performed on Jan. 14, 1936 (see Table II).

Nephrotic Glomerulonephritis.—Patient 5, aged twenty years, was admitted to the hospital on May 8, 1935, in her first pregnancy. She was approximately sixteen weeks pregnant. In January she had an unusually severe respiratory infection with a sore throat, after which she complained of nocturia and marked vomiting during February. The vulva had been swollen for one week. The swelling decreased slowly (Fig. 1). There was no other edema at any time. Ophthalmoscopic examinations on May 14, 21, and June 5 were normal. A vaginal hysterotomy was performed on June 4, 1935. On June 19, a diagnosis of bilateral retinopathy was made.

TABLE I. No. 11, LIPOID NEPHROSIS

DATE	WT. KILO.	B.P.	EDEMA	HB. GM. %	HEM. %	SERUM PROTEIN	A:G RATIO	N.P.N. MG. %	CHOLESTEROL	URINE ALB.	URINE CASTS	URINE R.B.C.
1/14/27	67.3	154/ 90	+ + + +		29	3.2	1.0	30	560	2.0	0	0
a. 3/30/27	51.0	120/ 70	+	11.0	35	3.7		28	510	0.4	+	+
b. 6/15/27	55.7	150/ 75	+ +	10.3	31	3.4		37	466	0.4	0	0
2/ 7/28			+ +	13.5	34	3.5		33	500	0.4	0	0
3/ 2/32	48.0		0	12.3	36	5.6	1.3	89	390	0.7		
c. 10/26/34		190/120		5.8	14	5.4	1.1	200	256	0.6		

a, Spontaneous abortion on 2/27. b, Hysterotomy and sterilization on 6/18. c, Died in December, 1934.

TABLE II. No. 1, ACUTE GLOMERULONEPHRITIS

DATE	WT. KILO.	B.P.	EDEMA	HB. GM. %	HEM. %	SERUM PROTEIN GM. %	A:G RATIO	N.P.N. MG. %	UREA MG. %	URINE ALB.	URINE CASTS	URINE R.B.C.	URINE U/B	URINE STAND. CLEAR. %
9/11/33	48.8	154/ 90	+	11.0	30	5.3	1.3	27	15	+ + +	+ + +	+ + +	29	57
a. 10/10/33	49.1	160/100	+	9.7	28	5.7		32	17	+ +	+ + +	+ + +	24	25
10/23/33	51.0	130/ 90	+	7.7	23	5.8		22	10	+ +	+	+	24	40
11/21/33	49.2	145/100	+ +		31	5.9		25	14	+ +	+	+ +	12	38
b. 10/ 9/34	51.0	114/ 70	+	12.4	38	5.4	1.1	29	15	0.5%	+	?	33	100
11/ 6/35	51.7	170/115	+ +	13.2	39	5.9	1.7	27	14				15	57
12/17/35	51.2	160/110	+ +			6.6		29	11	0.3%	0	0		
c. 1/13/36	52.0	155/100	+ +	11.5	35	5.1	1.6	26	15	0.4	+ +	0	31	52
1/28/36	48.5	140/100	+	13.4	43	5.8	1.5	43						

a, Therapeutic abortion. b, Double protein intake. c, Therapeutic abortion. 1/28/36 = cholesterol—490 mg. %.

TABLE III. No. 6, NEPHROTIC FORM OF GLOMERULONEPHRITIS

	DATE	WT. KILO.	B.P.	EDEMA	HB. GM. %	HEM. %	SERUM PROTEIN GM. %	A:G RATIO	N.P.N. MG. %	UREA MG. %	URINE ALB.	URINE CASTS	URINE R.B.C.	URINE U/B	URINE STAND. CLEAR. %
	5/ 8/35	58.5	140/ 68	+ + + +	9.3	23	4.6		46	31	+ + + +	+ + +	+ +	21	48
	5/20/35	62.7	130/ 80	+ + + +	6.3	22	4.4	1.6	54	34	+ + + +			22	41
a.	6/ 3/35	64.0	130/ 80	+ + + +	7.7	23	4.8		57	52	1.0	+ + +	+	15	28
	6/ 7/35		160/ 90	+ + + +	10.0	28	4.9		63	41	1.7%	+ +	+	12	32
b.	6/27/35	60.3	185/105	+	12.2	36					+ + +	+ +	+		
c.	6/30/35		180/110	+ +			4.1	1.8	49	24	+ + + +	+ + +	+	29	43
	12/23/35	55.1	180/100	+ +			4.9	0.7	48	28	2.0%	+ + + +	0	14	24

a, Therapeutic abortion. b, Discharge. c, Readmission with convulsions.

Three small blood transfusions were given because of an anemia. She was discharged from the hospital on June 27. Following her discharge she remained in bed, and on June 30 she complained of a severe headache followed by vomiting. She soon became stuporous and had a convulsion with coma. On readmission to the hospital she was drowsy, edematous, and had a blood pressure of 180/110. A few minutes afterward she had an acute generalized convulsion. She was transferred to the medical service and was discharged by them on July 14, 1935. Contraceptive instructions were given to the patient. On Dec. 16, 1935, her blood pressure was 180/100. During the first admission to the hospital the determined oncotic pressure on two occasions was 11.4 (calculated 15.5) and 17.2 cm. (calculated 19.0) of water. She would not eat all of the high protein diet. As much as 21 gm. of protein was excreted in the urine per twenty-four hours. This case was diagnosed as glomerulonephritis of the nephrotic type (see Table III).

Recurrent Acute Glomerulonephritis.—Patient 6, aged nineteen years, was seen on the surgical service on Feb. 22, 1933, because of nausea and vomiting. Her blood pressure then was 120/94. The urine contained albumin two-plus, hyaline casts, and the nonprotein nitrogen was 40 mg. per cent. A urea clearance at this time showed 52 per cent of normal. The renal symptoms were thought to be due to the dehydration. On April 16, 1935, when the patient was six weeks pregnant, she was seen in the prenatal clinic. At this time the blood pressure was 140/90 and the urine contained albumin two-plus, with hyaline casts. A therapeutic abortion was contemplated but the patient developed German measles, and by the time she recovered, pregnancy was well advanced. The albuminuria persisted and the blood pressure, despite treatment, gradually increased to a peak of 220/150 on Oct. 18, 1935. The patient gained 13 kg. in weight, and although she was not at term until November 6, an elective cesarean section with sterilization was performed. The urine at this time contained a large number of erythrocytes which persisted until the last examination on Dec. 6, 1935. At this time her blood pressure was still 200/140. It is possible that this patient had an essential hypertension, with a superimposed acute nephritis at term. However, in view of the history, symptoms, and signs at the time of delivery and their persistence over a period of six weeks, a more likely diagnosis would be a chronic glomerulonephritis with an exacerbation caused by the pregnancy (see Table IV).

The four patients whom we have described so far all have had varying degrees of hypertension, proteinuria, and edema. The last patient developed a hypertension early in pregnancy, without any other symptoms, which persisted after delivery. A résumé of the history is included for comparison.

Essential Hypertension.—Patient 91383, aged twenty-three years, was first seen on Oct. 5, 1933, at which time her blood pressure was 110/80 and the urinalysis was negative. She was approximately nine weeks pregnant. On Oct. 28, 1933, her blood pressure was 170/105 and remained high. On Feb. 25, 1934, she had a spontaneous delivery of a living infant weighing 1,100 gm., and a partial abruptio placentae. On June 5, 1934, her blood pressure was still 220/150, and on September 4 an abdominal hysterotomy and sterilization were performed for a six weeks' gestation. On September 28 the blood pressure was 240/126. Ophthalmoscopic examination on February 28 was negative, but on September 3 there was a definite neuroretinitis. The urea clearance on repeated examinations has been between 50 and 60 per cent of normal, and the urine has never contained albumin, casts, or blood. On July 12, 1935, the patient's family physician stated that she was having a persistent epistaxis. This patient undoubtedly has a malignant hypertension which has been accelerated by the pregnancy.

Acute Glomerulonephritis With Death.—Patient 55019, aged twenty-two years, gravida v, para iv, was admitted on Feb. 15, 1932, approximately twelve weeks pregnant. She noticed edema of her legs for ten days and of her hands for one day,

TABLE IV. No. 6, RECURRENT ACUTE GLOMERULONEPHRITIS

DATE	WT. KILO.	B.P.	HB. GM. %	HEM. %	SERUM PROTEIN GM. %	A:G RATIO	N.P.N. MG. %	UREA MG. %	URINE ALB.	URINE CASTS	URINE R.B.C.	URINE U/B	URINE STANDARD CLEARANCE %
4/25/35	50.8	140/90		35			25	11	+ +	+ +	0	45	61
7/29/35	57.5	150/100	11.9	34			26	13	0.1	+	0	59	85
9/26/35	63.0	168/123	12.9	33	6.8	2.0	27	12	0.3	+ + +	+	35	39
a. 10/21/35	63.2	190/150	12.6	40	7.7	1.3	27	14	0.6	+ + + +	+ + +	35	45
b. 11/25/35	51.8	190/150	15.7	45	7.9	2.0	38	15	0.2%	+ + +	+	28	49
12/ 6/35	52.7	200/140							+ + +	+ +	+		

a, Cesarean section and sterilization. b, Hypertensive encephalopathy.

TABLE V

NUMBER	AGE	GRAVIDA	MINIMAL WEIGHT (KILO.)	WEIGHT LOSS (KILO.)	ETIOLOGY AND DURATION OF SYMPTOMS	DURATION OF PREGNANCY WEEKS	TERMINATION OF PREGNANCY	BLOOD PRESSURE	EDEMA	URINE			HEMOGLOBIN GM. %	SERUM PROTEIN GM. %	CHOLESTEROL MG. %	N.P.N. MG. %
										ALBUMIN	SEDIMENT CASTS	SEDIMENT R.B.C.				
					Acute Glomerulonephritis											
1	20	i	50	2	Edema for 5 weeks	17	T. A.	140/90	+ +	+ + + +	+	+	11.0	5.3	270	27
2	18	i	46	11	Hematuria for 3 months	28	Spon. term	152/100	+ +	+ + + +	+	+	12.2	6.8	464	27
3	22	v	58		Diphtheria and nephritis 6 weeks	13	Abortion	160/120	+ + +	+ + +	+	+	5.5	5.7	293	53
					Nephrotic Form of Glomerulonephritis											
4	16	i	40	16	Edema for 3 weeks Edema of *labia*	23	Abortion	200/150	+ + + +	1.8%	+	0	12.6	4.2	*526	31
5	20	i	52	12	Cold, 4 mo. previous Edema of *labia*	16	T. A.	180/110	+ + +	+ + +	+	+	5.5	4.2	298	63
					Recurrent Acute Glomerulonephritis											
6	19	i	51	13	Albumin and hypertension 6 months	10	C. S. + S.	200/140	+ +	+ + +	+	+	15.2	6.8		27
7 ?	38	viii	69	6	Hypertension since 1931	18	T. A.	260/135	+ +	0.7%	+	+	13.8	6.1		35
8	26	iv	43		Acute nephritis 6 months previous	14	T. A. + S.	125/70	+	+ + + +	+	+		6.4		30
9	20	i	43	2	Nephritis 3 years Edema of eyes 1 year	17	T. A. + S.	205/110	0	+	+	+	11.0	6.9		41
					Lipoid Nephrosis											
10	17	i	59	19	Headache and edema of *labia* 1 month	38	Spon. term	190/150	+ + + +	2.5%	+	+				40
11	22	i	48	19	Erysipelas 1 year Edema for 2 months Edema of *labia*	18 †10	Abortion T. A. + S.	154/90	+ + + +	2.0	+	0	9.0	3.2	560	30
12	16	i	50		Edema 1 month	37	Spon. term	170/125	+ +	1.2	0	0	11.0	5.4	511	30

T.A., Therapeutic abortion. S., Sterilization. Spon. Term., Spontaneous labor at term. C.S., Cesarean section.
*Total lipid = 2018 Mg. %.
†Second pregnancy.

hematuria for six weeks, and vomiting for three months. In January she had had diphtheria and the urine was colored at that time. The hemoglobin estimation was 5.5 gm. per cent, serum protein 5.7 gm. per cent, nonprotein nitrogen 53 mg. per cent, and blood urea nitrogen 32 mg. per cent. A diagnosis of acute glomerulonephritis was made. Several blood transfusions were given. On February 24 marked dyspnea and coma were present, and on February 25 she aborted. Death occurred on March 1. The autopsy findings were: acute glomerulonephritis, extensive thrombophlebitis of both ovarian and popliteal veins, infarcts of both lungs, and embolism of the pulmonary arteries. The nephritis, which was the cause of the anemia, was undoubtedly the primary cause of the extensive thrombophlebitis.

Pertinent data from the patients in this series are listed in Table V. These cases have been collected over a period of twelve years, during which time approximately 22,000 patients have been delivered. All of the patients, with but one exception, were young. Edema was the complaint of 6 on admission. We were able to determine a possible etiology in only 4 of the cases. In 9 of the patients the disease was noted before the twentieth week of pregnancy; 4 patients went to term, but therapeutic abortion was prevented by other factors in one case. There were 3 spontaneous abortions and 6 therapeutic abortions. Four patients were sterilized. The increased blood pressure in the patients with lipoid nephrosis was thought to be caused by the pregnancy because of the rapid decrease after delivery, although the other symptoms persisted. The serum protein concentration was unusually low in the patients with nephrosis. Hypercholesterolemia was present in 4 out of 7 patients, anemia was marked in 3, and a nitrogen retention was present in 2.

The edema was usually general, and in the patients with nephrosis there was an associated hydrothorax and ascites. Marked edema of the labia was present in 4 out of 5 of these patients.

The excretion in the urine of large amounts of protein over a long period of time is characteristic of the nephrotic cases. The high concentration of 1.8 to 2.5 per cent for the twenty-four-hour period is striking.

Erythrocytes and various types of casts were present on repeated examination of the urine in those patients with a plus mark in the proper column.

DISCUSSION

Normal pregnancy is characterized by a tendency toward edema, slight albuminuria and a retarded elimination of water. Elden and Cooney, in a small series of normal pregnant women, have noted that the Addis count is higher than in normal nonpregnant individuals. Dieckmann and Wegner and other observers have described the relative anemia, decrease in serum protein concentration, hypercholesterolemia, and lipemia seen in normal pregnancy. Epstein has mentioned pregnancy as a cause of lipoid nephrosis, but in a personal communication in 1927, he was unable to point out a definite relationship. Several cases of nephrosis have been reported in which the onset was dated from a

pregnancy. The tendency toward edema, albuminuria, faulty water elimination, and abnormal fat metabolism observed in normal pregnancy is characteristic of nephrosis. It would seem reasonable that the symptoms of a nephritis or a nephrosis, if it developed during pregnancy, would be made worse because of the changes incidental to the latter condition. In our cases this was certainly true.

Numerous tests have been devised for determining the function of the kidneys. These have been reviewed in a previous article, where it was pointed out that pregnancy per se causes very definite alterations in these various tests. The urea clearance test in pregnancy has a prognostic or diagnostic value only if there is a constant clearance of less than 50 per cent of the normal, with a urine volume of 1 c.c. or more per minute, or if there is a persistent decrease, as in the first case described. The presence of protein in the urine is only suggestive of nephritis, and may be caused by cystitis, pyelitis, or a nephrosclerosis. Similarly, the presence of hyaline or granular casts is not indicative of nephritis. They may or may not be present in proved cases of chronic nephritis. Erythrocytes in the urine may be due to renal stone, tuberculosis, tumor, or to hydronephrosis with intermittent capillary ruptures. Hematuria may also occur if there is a marked increase or decrease of the blood pressure, as seen not infrequently in the toxemias of pregnancy. However, in these patients it is present for a few hours or a day at the maximum. What are the criteria necessary for a diagnosis of acute nephritis? These have been mentioned in the definition given for this condition, but we wish to emphasize the persistence of the erythrocytes in the urine for a period of a week or longer as evidence of acute glomerulonephritis. Likewise, the persistence of edema and albuminuria, despite the delivery, is indicative of a nephrosis.

In a period of four years, 398 microscopic examinations of catheterized specimens of urine were made by the author in 450 clearances; 100 patients with abnormal urine findings were found. A modification of the Addis technic was used and the number of erythrocytes was increased and found over a period of one week or longer in the urine specimens of 41 patients. Eight of these, Nos. 1, 2, 3, 5, 6, 7, 8 and 9, an incidence of 0.05 per cent, were diagnosed as "acute or recurrent acute glomerulonephritis." In the remainder, the transient hematuria was thought to be due to a "pregnancy toxemia." Casts were found in the urine of 48 patients.

Questionnaires were sent to 12 physicians in charge of large obstetric services or of large groups of patients with nephritis. Six replies were received, but only 3 contained data which could be used.

Mussey and coworkers of the Mayo Clinic have been able to group their toxemias of pregnancy according to the classification of nephritis used by Volhard and Fahr. In a recent communication Mussey reemphasized their beliefs and stated that "practically all of the 'acute nephritis' accompanying pregnancy is a part of the

toxemic picture and is merely a local manifestation of this condition.'' They observed one patient who, as a child, had an acute glomerulonephritis, recovered, and later in life went through pregnancy with no evidence of nephritis or toxemia.

Wegner of the Washington University has kindly permitted the use of the following data which he is preparing for an article on lipoid nephrosis. During the period in which 10,596 deliveries occurred, there were 6 patients with acute glomerulonephritis and 3 with lipoid nephrosis, an incidence of 0.056 and 0.028 per cent, respectively. In all of the cases the renal condition seemed to be exacerbated as pregnancy advanced. There was 1 therapeutic abortion, 5 premature labors (3 induced and 2 spontaneous), and 3 deliveries at term. He had 1 patient who went through an uneventful pregnancy after an acute glomerulonephritis. Two patients who had had acute nephritis died, and of those with nephrosis, 1 died, thus giving a mortality rate of 33.3 per cent for each condition.

Eastman, of the Johns Hopkins University Hospital, stated that during a ten-year period they had 16,150 admissions to the hospital, 10,965 deliveries, and 641 cases of chronic nephritis. In the nephritic group there were 2 cases of acute nephritis during pregnancy and 3 cases of questionable lipoid nephrosis. The incidence is 0.018 and 0.027 per cent, respectively.

Barach and Boyd treated a twenty-year-old patient with nephrosis, using various procedures, and finally reported that after 295 gm. of gum acacia had been injected intravenously over a period of four weeks, there was a clinical cure. Two years after the injection of the acacia the patient passed through an uneventful pregnancy and puerperium and was in an excellent condition six months after the delivery.

Addis, in his monograph on nephritis, lists 2 patients out of a total of 72 in whom a ''pregnancy toxemia'' may have been the cause of the arteriosclerotic Bright's disease which caused their deaths, twenty-two and seven years, respectively, after the pregnancy. In a third case, pregnancy may have been the cause of a hemorrhagic Bright's disease which he studied during the terminal stage. A fourth patient, who had a terminal hemorrhagic Bright's disease, became pregnant twice but was always aborted.

Murphy and coworkers, in a recent analysis of 94 cases of diffuse glomerulonephritis, stated that in 16 cases (17 per cent) pregnancy was the only etiologic factor that they could find. Six of these patients recovered, 7 became chronic, and 3 died. They stated that ''our autopsy studies in connection with these cases lead us to believe that acute diffuse glomerular nephritis due to eclampsia is practically the same as that due to other causes.'' They also stated that ''the acute phase of glomerular nephritis may be so mild that it passes unrecognized, and no indication of renal damage is observed until the disease has progressed into the chronic stage, when renal insufficiency sets in.''

Volhard lists pregnancy as the cause of the acute glomerulonephritis in 4 cases, and Lichtwitz in 2, according to Fishberg.

The author has observed one patient through an uneventful pregnancy two and one-half years after a classical acute glomerulonephritis. During the acute stage of the nephritis the blood pressure was 170/110 and convulsions occurred. Another patient who had had a classical acute nephritis in 1920 was aborted and sterilized in 1928. She was pregnant in 1923, 1925, and 1928 and uremia developed with each pregnancy. Death occurred in 1930. The autopsy confirmed the diagnosis. Many other patients with histories of previous acute nephritis have been studied. Renal impairment may or may not be present.

It is obvious that if acute nephritis may be of only a few days' or weeks' duration, many of our cases of preeclampsia and eclampsia should be so classified. Furthermore, if there are varying degrees of nephrosis, as determined by the degree of edema and albuminuria and the level of the serum protein concentration, it is obvious that many of our preeclamptic patients have a nephrosis. If pregnancy can be considered the etiologic agent of nephritis, then the high incidence of permanent vascular renal damage noted by various observers, especially in preeclamptic patients who are treated expectantly for weeks, may be attributed to the nephritis. Repeated examinations of the urine, especially microscopic examination of the sediment, are necessary to diagnose properly the condition. In certain cases, serum protein determinations will be of inestimable value.

DIAGNOSIS

The differential diagnosis of acute glomerulonephritis or lipoid nephrosis from preeclampsia is difficult. Acute nephritis and nephrosis occur more commonly in the first half of pregnancy, in contrast with preeclampsia, which occurs in the last trimester. The edema in preeclampsia may be general, but, as a rule, it differs in that it tends to be in the dependent portion of the body. In the toxemias of pregnancy the edema may disappear with proper treatment, while in the acute nephritis and nephrosis it is, on the whole, more resistant to treatment. After delivery there is a rapid elimination of the edema in preeclampsia and eclampsia which does not occur in the other conditions. The persistence of erythrocytes in the urine for longer than one week would exclude a preeclampsia. The excretion of protein in the urine in preeclampsia and eclampsia rarely exceeds 10 gm. per day, and is usually less than 5 gm. per day. In the presence of an oliguria the concentration may reach 5 per cent. In acute nephritis and nephrosis the protein excretion is quite marked, uninfluenced by treatment and especially not decreased by delivery. A serum protein concentration of less than 5 per cent before delivery, or of less than 5.5 per cent two weeks after delivery, would strongly suggest a nephrosis.

TREATMENT

Edema.—Diuretics have been of little value during pregnancy. A diet consisting of fruits and fruit juices has given excellent results, but should not be used longer than ten days. If there is a hydrothorax and ascites, the intake, especially if the fruit juice diet is used, should be limited to 1,000 or even 800 c.c. per twenty-four hours. The maintenance diet should contain as little sodium and chloride as possible. Sodium sulphate by mouth as a hydragogue cathartic is nontoxic and just as efficacious as magnesium sulphate. If the patient's serum protein is less than 5 per cent, or the serum albumin is less than 2.5 per cent,

transfusions of blood or plasma are indicated. Intravenous injections of gum acacia may be necessary to raise the oncotic pressure above the edema level. Thyroid extract has been of no value.

Proteinuria.—The protein found in the urine is chiefly albumin. No therapy has prevented or reduced its elimination. Sufficient protein should be ingested to supply the basal need, as well as to balance that lost in the urine. Carbohydrate spares protein; therefore, the caloric need should be supplied chiefly by it. It is usually difficult to force these patients to consume enough of the diet to be of any value. Vitamins B and G have been of some value in stimulating the appetite and aiding absorption.

Hematuria.—If the hemoglobin decreases below 11 gm. per 100 c.c. of blood, transfusions and iron salts are indicated.

Hypertension, Oliguria, Convulsions.—The usual treatment for eclampsia, namely, hypertonic glucose or sucrose, phenobarbital sodium, magnesium sulphate solution intramuscularly, morphine, chloral hydrate and, occasionally, venesection and lumbar puncture, should be instituted.

Pregnancy.—Pregnancy should be terminated if the symptoms and signs increase in severity. It should be interrupted without hesitation, as soon as it can be done safely, if there is no improvement in the nephritis or nephrosis, unless the addition of two or three weeks of intrauterine life will offer the baby a better chance of survival. It must be remembered that if the pregnancy is permitted to continue, intrauterine death and abortion are likely to occur. If a patient has had an acute nephritis and has recovered completely, as indicated by a negative urinalysis and normal renal function test, there is no reason why she should not be permitted to become pregnant, or if pregnancy occurs, why it should not be permitted to continue.

CONCLUSIONS

1. Acute glomerulonephritis and lipoid nephrosis of the classical type are rare complications of pregnancy. The incidence is less than 0.05 per cent.

2. These conditions are found most frequently in young primiparas in the first half of pregnancy.

3. Spontaneous abortion is a frequent occurrence.

4. Therapeutic abortion is indicated if the disease is present before the thirtieth week of pregnancy and shows no improvement in a period of two weeks. If it occurs after this time, temporization is warranted in an endeavor to obtain a viable baby.

5. The chief difference between classical glomerulonephritis and preeclampsia is the persistence of the hematuria in the former, and the rapid amelioration of the other symptoms after delivery in the latter.

6. Lipoid nephrosis differs from preeclampsia, as a rule, only in the degree of the various symptoms. After delivery the symptoms and signs of the former persist, while in the latter they subside.

7. Careful and repeated microscopic examinations of the sediment of the urine (Addis technic) from toxemic patients is of inestimable value in making a proper diagnosis.

8. A history of acute glomerulonephritis or lipoid nephrosis is not a contraindication to pregnancy, provided complete recovery has occurred.

REFERENCES

Addis, T., and Oliver, J.: The Renal Lesion in Bright's Disease, 1931, New York, Paul B. Hoeber. *Barach, J. H.:* Personal communication. *Barach, J. H., and Boyd, D. M.:* Am. J. M. Sc. **189:** 536, 1935. *Dieckmann, Wm. J.:* Am. J. Obst. & Gynec. **19:** 706, 1930. *Idem:* Am. J. Obst. & Gynec. **22:** 351, 1931. *Idem:* Am. J. Obst. & Gynec. **29:** 472, 1935. *Dieckmann, Wm. J., and Michel, H. L.:* Arch. Int. Med. **55:** 420, 1935. *Dieckmann, Wm. J., and Wegner, C.:* Arch. Int. Med. **53:** 71, 188, 353, 540, 1934. *Eastman, N.:* Personal communication. *Elden, C. A., and Cooney, J. W.:* J. Clin. Investigation **14:** 889, 1935. *Epstein, A.:* Personal communication. *Fishberg, A.:* Hypertension and Nephritis, Philadelphia, 1934, Lea and Febiger. *Leiter, L.:* Medicine **10:** 135, 1931. *Murphy, F., Grill, J., and Moxon, G.:* Arch. Int. Med. **54:** 483, 1934. *Mussey, R. D.:* Personal communication. *Rockwood, R., Mussey, R., and Keith, N.:* Surg. Gynec. Obst. **42:** 342, 1926. *Wegner, Carl:* Personal communication.

THE LOW OR CERVICAL CESAREAN SECTION*

An Analysis of the End-Results of an Additional 166 Operations

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ABDOMINAL delivery through the lower uterine segment was proposed by Frank, of Cologne, in 1907, because of his dissatisfaction with the results of the classical cesarean section, especially in women who had been long in labor and were infected or presumably infected. While this method soon found adherents in Germany, it received but little consideration elsewhere. In the United States, this procedure was seldom mentioned until 1915. Since then it has become firmly established as a standard procedure and has replaced or is gradually replacing the classical or corporeal cesarean section in many important obstetric clinics. My own interest was aroused early. At first I reserved the cervical operation for the poor risks and for the neglected cases, performing the classical operation on those women who were considered to be in good condition for an abdominal delivery. As time went on it became possible to observe repeatedly that the neglected parturient, delivered through the lower segment, convalesced much more satisfactorily than did her fellow patient considered a good surgical risk and delivered by the Sänger operation. It was equally noticed that following the low or cervical cesarean section high thermic elevation, high pulse rate, and

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abdominal distention—conditions which were frequently met after the classical cesarean section—were the exception rather than the rule. With these points clearly in mind, it was decided to give all women who needed an abdominal delivery the benefit of this newer method, and it has been employed consistently since.

My previous publications have emphasized that the lower uterine segment may be reached in one of three ways in performing cesarean section: (1) by the extraperitoneal route as in the Latzko operation; (2) by the transperitoneal route, sometimes referred to as peritoneal exclusion, illustrated by the Veit-Fromme-Hirst technic; and (3) by the intraperitoneal approach as in the popular method of doing the low or cervical cesarean section today. This last operation, as it is now executed, has reached its present stage of perfection through several additions and modifications in technic by numerous obstetricians. Unfortunately space does not permit me to mention all their names. Suffice it to say that in its performance the bladder is separated from the uterus, an upper flap of peritoneum may or may not also be separated, an incision is made in the lower uterine segment, and after delivery the sutured lower segment incision is entirely covered by the bladder so that it becomes retrovesical, retroperitoneal, or subperitoneal, whichever term one prefers to use.

In September, 1926, I[1] presented a paper entitled "The Obstetric Future of Women Delivered by the Low or Cervical Cesarean Section," at the Chicago meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons. Up to that time a longitudinal incision in the lower portion of the uterus had always been used. Forty-one repeated cervical cesarean sections with firmly healed scars and the impossibility of locating the previous line of incision were reported. The first patient admitted to my service for a repeat cervical cesarean section, upon my return, had been in hard labor for eleven hours. A longitudinal incision of the segment had been made at her previous intervention and, because of a large fetus, the incision had been extended upward in the body of the uterus. Upon reopening the abdomen by resecting the previous abdominal scar and upon again separating the bladder, a weak spot, about 3 cm. in circumference, was found in that part of the incision which had extended in the musculature, the edges of the scar in that area being separated and held only by peritoneum, while the lower part of the incision which had been placed in the lower uterine segment was intact and perfectly healed. A longitudinal incision was then made, and during its closure the defective portion of the scar was repaired; finally the bladder peritoneum was sutured to the uterus in such a way as to cover completely the incision.

On the basis of these findings it occurred to me that if under any and all circumstances an incision could be placed entirely in the lower segment, the incidence of weak scars could be even more definitely reduced.

Kehrer, in 1881, was said to have advised a transverse incision. Kerr and Hendry[2] reported 107 conservative cesarean sections by the lower segment incision. They state: "The uterine incision described in this article is made in a transverse direction so that there is ample space in which to open the lower uterine segment without disturbing the bladder." To avoid damage to the large vessels at the side of the uterus they advise curving the incision with the convexity directed downward. Anatomically, and according to their illustrations, the incision is placed above the bladder attachment on the uterus, therefore at the isthmus or junction of the lower segment and corpus rather than in the lower segment itself. My own experience has taught me that the zone of the lower segment cannot be reached definitely without separating the bladder.

The operation which I have described as the transverse cervical cesarean section[3, 4] was devised in 1926. In this operation the bladder is separated from the uterus, a curved (half moon) incision with the convexity directed toward the symphysis pubis is placed entirely in the lower segment and is covered subsequently completely by the bladder. The transverse cervical cesarean section offers certain definite advantages, namely: (1), it avoids encroaching upon the uterine musculature and allows the placing of the incision entirely in the lower segment; (2), the bladder separation does not have to be carried as far downward as is the case with the longitudinal incision; and (3), repeated operations are simpler to perform.

M. Reeb,[5] of Strasburg, a protagonist of the low cesarean section, recently stated in a paper entitled "A propos des fistules urinaires après la césarienne basse" that in the 415 low cesarean sections performed at the Strasburg clinic since 1908 he had observed three urinary fistulas, two vesicocervical and one vesicovaginal.

CERVICAL CESAREAN SECTIONS

TABLE I. TYPE OF OPERATION

Transverse cervical cesarean section	160
Peritoneal exclusion (Veit-Fromme-Hirst)	6
	166

TABLE II. NUMBER OF PREGNANCIES

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
Para i	55	5
Para ii	48	1
Para iii	36	
Para iv	9	
Para v	4	
Para vi	5	
Para viii	1	
Para x	2	
	160	6

These followed repeated cesarean sections in two cases and the third was complicated by a paravesical cyst injured during the intervention. Secondary operation was successful in all three cases and healing took place by first intention. In his paper the author asks if modification of technic, giving up a laborious separation of the bladder, substituting eventually, in cases of repeated cesarean, a transverse incision for the usual longitudinal, would not make these lesions even more infrequent.

Thus far, in my hands, urinary fistulas, following the low or cervical cesarean section, have not occurred. I feel strongly, however, that if a

TABLE III. LABOR

TRANSVERSE CERVICAL FORTY-THREE PATIENTS HAD LABOR			PERITONEAL EXCLUSION SIX PATIENTS HAD LABOR		
HOURS	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION	HOURS	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
2¾	1		22	1	
3	2		23		1
4	4		24	2	
6	3		25	1	1
7	2		26	2	
8	2		27	1	
9	2		29½	1	
11	1		32		1
12	1	2	36	1	
14	1		38½	1	
15	1		39	1	
17	1		48	1	
18	1	1	Few hours	1	
19	1		Slight labor	1	
20½	1		Vague labor	4	
21	1				

TABLE IV. MEMBRANES

HOURS RUPTURED	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION	HOURS RUPTURED	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
2	1		17	1	
2¾	1		18	1	
7	2		21	1	
8	1		23	1	
10	1		24	1	1
11	1		26	1	
12	1		32		1
15	1		48		1
Few hours	2		Hours not determined	4	

Membranes ruptured in 3 patients of the peritoneal exclusion group.
Membranes ruptured in 21 patients of the transverse cervical group.

transverse incision makes a repeated operation easier, a point which I have frequently emphasized, and if it avoids bladder injuries on account of the less laborious separation of this organ, by the same reasoning these advantages should apply to the first or initial low cesarean section.

I have personally performed 584 cervical cesarean sections using all the methods of approach to the lower uterine segment. The first 418 were reported in a paper read before the American Association of Obstetricians, Gynecologists and Abdominal Surgeons at the Niagara Falls

TABLE V. CERVICAL DILATATION

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
Fully dilated	2	
Half dilated	1	2
Dilated to admit 4 fingers	1	
Dilated to admit 3 fingers	5	
Dilated to admit 2 fingers	5	2
Dilated to admit 1 finger	7	
Dilatation not stated		2
	21	6

In the other 22 women who had labor and who were delivered by the transverse cervical cesarean section, the amount of cervical dilatation was not noted.

TABLE VI. VAGINAL EXAMINATIONS

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
2 Vaginal examinations at home		1
1 Vaginal examination at home	1	
1 Vaginal examination in hospital	3	2

Eight vaginal examinations were done on 7 patients. The small number of vaginal examinations is accounted for by the fact that I conduct my own labor cases by means of rectal examinations and that the same rule is enforced on my service.

TABLE VII. INDICATIONS

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
Previous cervical cesarean section	63	
Previous classical and cervical cesarean sections	1	
Previous classical cesarean section	5	
Cephalopelvic disproportion	35	4
Central placenta previa	7	
Marginal placenta previa	2	
Abruptio placentae	2	
Previous vaginal plastics and uterine suspension	10	
Previous vaginal plastics (Including cervical amputation)	4	
Repaired complete perineal laceration	3	
Toxemia of pregnancy	2	
Chronic nephritis	1	
Mitral heart disease	6	
Cervical dystocia	6	1
Myomectomy during pregnancy	2	
Myomectomy, multiple	1	
Frank breech, generally contracted pelvis	5	
Spondylolisthetic pelvis	1	
Nagele pelvis	1	
Congenital hip disease	1	
Dystocia-dystrophy syndrome	2	
Justo-minor pelvis		1
	160	6

NOTE: In several of these patients there was more than one indication. Only what was thought to be the most important indication was noted in this table.

The indication was a previous cesarean section in 69 or 41.5 per cent of the patients.

meeting in September, 1930.[6] The cervical scars of four uteri, later removed for other pathologic conditions, likewise were studied and reported.[7]

Since reporting the first 418 cervical cesarean sections which had been performed in 31 hospitals, 166 additional operations, 160 trans-

TABLE VIII. ANESTHESIA

TYPE OF ANESTHESIA	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
Local	17	
Spinal	3	
Avertin, nitrous oxide, oxygen	65	1
Avertin and local	1	
Nitrous oxide, oxygen, ether	74	5
	160	6

NOTE: For local anesthesia 1 per cent novocaine solution was used. For spinal anesthesia 120 mg. of novocaine crystals dissolved in spinal fluid were employed. The dose of avertin varied from 60 to 100 mg. per kilo of body weight. The average dose was 80 mg. This form of anesthesia is contraindicated in hepatic and renal disorders.

TABLE IX. COMPLICATIONS

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
Preoperative:		
Upper respiratory tract infection	1	
Anemia of pregnancy (severe)	1	
Ablation of ovarian cyst with twisted pedicle during pregnancy	1	
Myomectomy for necrobiosis during pregnancy	1	

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
Postoperative:		
Sepsis of abdominal incision	5	1
Lochiometra	4	2
Pyelitis	4	1
Pyelitis and vesical distention	1	
Gastric dilatation requiring lavage	3	1
Upper respiratory tract infection	5	
Phlebitis (left)	5	
Puerperal psychosis	1	
Alveolar abscess, Temp. 105° F.	1	
Puerperal sepsis, Temp. 105° F.	1	
Frontal sinusitis and carious tooth	1	
Dehiscence of abdominal incision	1	

Blood transfusion was resorted to six times on five patients.

verse cervical cesarean sections and 6 Veit-Fromme-Hirst peritoneal exclusions have been performed in 21 hospitals. Peritoneal exclusion is resorted to in women who have had long labors, ruptured membranes, vaginal examinations, and sometimes attempts at delivery by forceps. The 166 operations mentioned form the basis of this paper, and, for the sake of clearness, are presented in tables.

CASE REPORT

One patient in this group has an interesting history. Mrs. M. F., forty years old, para xii. Her first child, a male infant, was delivered normally in her home in 1917 and died at four and one-half months. A female child was delivered normally in her home a year later. Her third child, a ten-pound boy, and her fourth child, a female infant, were also delivered normally in her home. The fifth pregnancy ended in an eight weeks' miscarriage which was followed by a curettage. She was admitted to my service at the end of her sixth pregnancy. She was then twenty-nine years of age. She had a hemorrhage from a partially separated placenta and was not in labor. On Aug. 30, 1922, she was delivered by a Veit-Fromme-Hirst peritoneal exclusion of a female child who lived. Her puerperium was complicated by gastric dilatation and a myocardial disorder; she nonetheless made a good

TABLE X. MATERNAL MORTALITY

There was one maternal death in 166 cases or 0.6 per cent. This patient was a quartigravida, her first pregnancy having terminated in a miscarriage and her second in the delivery of a macerated fetus. Her third pregnancy was complicated by chronic nephritis, edema, and asthma. She was delivered on April 17, 1931, by a transverse cervical cesarean section of a male child who did well. During her fourth pregnancy she developed a hernia of the gravid uterus, the chronic nephritis and emphysema became accentuated, a second transverse cervical cesarean section was performed at term, on Aug. 11, 1932, and she was again delivered of a male child who lived. On August 12 she developed a paralytic ileus which was controlled by a jejunostomy performed under local anesthesia. She died of chronic nephritis, bronchitis, emphysema, and myocarditis thirty-six hours after operation.

TABLE XI. BABIES

169 babies were born, there being 3 sets of twins. Of these 78 were males and 91 females.

One male child had spina bifida and was operated on successfully. One male child weighed 13 pounds 13 ounces (6,298.5 grams).

Fetal Mortality

169 babies were born, 8 of whom did not survive, an uncorrected fetal mortality of 4.7 per cent. This includes monsters, macerated fetuses, and stillborns.

Causes of Fetal Deaths

1. Macerated male fetus, second cervical cesarean.
2. Stillborn, male, autopsy showed congenital heart disease. First cervical cesarean. (Mother was 46 years old and had had extensive vaginal plastics and uterine suspension.)
3. Stillborn, female, central placenta previa. First cervical cesarean.
4. Underdeveloped male (2,280 grams); lived 24 hours. Second cervical cesarean.
5. Female twin, died of hemorrhagic disease. Third cervical cesarean.
6. Premature male, 8 months' gestation, lived 6 hours. Second cervical cesarean.
7. Premature female, 7 months' gestation, lived 4 hours. Fourth cervical cesarean.
8. Female monster (absence of anterior abdominal wall). Second cervical cesarean.

All the fetal deaths occurred in the transverse cervical cesarean group.

TABLE XII. REPEATED CERVICAL CESAREAN SECTIONS

Second operation	44
Third operation	20
Fourth operation	4
Sixth operation	1
	69

NOTE: In 5 of these cases the previous operation was a classical cesarean section performed by other surgeons. In the other 64 cases the previous operation was a cervical cesarean section.

A transverse cervical cesarean section may be done in subsequent deliveries, but the Veit-Fromme-Hirst peritoneal exclusion cannot be repeated.

recovery. Following this cesarean section she had three normal deliveries in the hospital, female children being born. She was admitted at the end of her tenth pregnancy with a placenta previa and hemorrhage and she was not in labor. She was delivered of a male child the same day, April 3, 1931, by a transverse cervical cesarean section, under local anesthesia. The lower segment was found intact and

TABLE XIII. PREVIOUS SCARS

SIXTY-NINE SCARS EXAMINED		
Cervical Cesarean Scars		
Cervical scar could not be identified in		54
Scar appeared as a hair line in		1
Scar appeared as a thin line in		3
Lower segment firm but irregular in areas in		1
Lower segment intact but thin in		1
Lower segment healed but thin at midpoint in (This was the sixth cervical cesarean)		1
Classical Cesarean Scars		
Previous classical cesarean scars encountered		8
Weak scar	1	
Healed scars	7	
All the healed scars appeared as depressions in the uterine wall.		
There were no ruptured scars in this series of cases.		

TABLE XIV. ADHESIONS IN THE REPEATED CERVICAL CESAREAN SECTIONS

Following the Veit-Fromme-Hirst peritoneal exclusion, a wide band of peritoneum extends from the cervix to the abdominal wall.	
In the transverse cervical cesarean group 30 had adhesions as follows:	
Lower segment adherent to abdominal wall	3
Bladder adherent to parietal peritoneum	7
One peritoneal band to abdominal wall	7
Two peritoneal bands to abdominal wall	4
Three peritoneal bands to abdominal wall	1
One omental adhesion	8
No intestinal adhesions were found in any of the patients.	

TABLE XV. PELVIC DELIVERIES FOLLOWING THE CERVICAL CESAREAN SECTION

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
One normal delivery (Seven months' macerated fetus)	1	
Two normal deliveries	2	
Three normal deliveries		1
Version and extraction (Twelve-hour labor)	1	
Miscarriage at 5 months	1	
Eight deliveries through the pelvis; six children survived.		

TABLE XVI. SUBSEQUENT OPERATIONS

1. Supravaginal hysterectomy, right salpingo-oophorectomy for a necrotic myoma.
2. Supravaginal hysterectomy, right salpingo-oophorectomy for necrotic cystic myoma and cystic right ovary.
3. Ablation of ovarian cyst with twisted pedicle during the sixth week of the third pregnancy. Two previous transverse cervical cesarean sections. Pregnancy went to term. Delivery by third transverse cervical cesarean section.
4. Vaginal plastics, supravaginal hysterectomy, double salpingo-oophorectomy for procidentia. Appendectomy.
5. Left salpingo-oophorectomy for endometriosis.
6. Porro cesarean section, right salpingo-oophorectomy for hemorrhage from placenta previa at second pregnancy.

contained no weak areas. Subsequent to the second cesarean section she had two normal deliveries in the hospital, resulting in the birth of a male and a female child, the last delivery occurring in 1934. She now has 10 living children, 3 boys and 7 girls.

SUMMARY AND CONCLUSIONS

This study is based on 166 additional cervical cesarean sections, 160 transverse cervical cesarean sections and 6 Veit-Fromme-Hirst peritoneal exclusions. They follow a previously published report of 418 cervical cesarean sections.

These 166 operations were performed by the author in 21 hospitals, varying in equipment from that of the well-regulated metropolitan maternity hospital, where a separate operating room is frequently maintained for cesarean section, to that of the small rural hospital where all surgery, clean and septic, including cesarean section, is performed in the same operating room.

Increasing evidence seems to prove that the cervical cesarean section fulfills the three main considerations advanced for it by its protagonists, namely: protection against septic peritonitis, better healing of the incision, and an easier convalescence.

There was one maternal death in the 166 operations, a gross maternal mortality of 0.6 per cent. This occurred in a quartigravida at her second cervical cesarean section. The cause of death was chronic nephritis, bronchitis, emphysema, and myocarditis.

One hundred and sixty-nine infants were born, 78 males and 91 females; 8 did not survive, an uncorrected fetal mortality of 4.7 per cent. This includes monsters, macerated fetuses, and stillborns (Table XI).

The cervical cesarean section may be repeated with ease. The highest number performed on one woman in this series was 6 (Table XII).

In 61 repeated cervical cesarean sections no ruptured scars were encountered and no intestinal adhesions were discovered.

There were 8 pelvic deliveries in 5 women. Six of the infants survived, 1 fetus was macerated, the other was a five months' miscarriage.

The transverse incision, in my hands, has proved to be more satisfactory than the longitudinal in performing the low or cervical cesarean section.

An adequate test of labor may be safely given in border line cases, thus allowing a number of women to deliver themselves through the pelvis who otherwise might have been delivered abdominally.

REFERENCES

(1) *Phaneuf, L. E.:* Am. J. Obst. & Gynec. **13**: 446, 1927. (2) *Kerr, J. M., and Hendry, J.:* Surg. Gynec. Obst. **43**: 85, 1926. (3) *Phaneuf, L. E.:* Boston M. & S. J. **197**: 825, 1927. (4) *Phaneuf, L. E.:* Surg. Gynec. Obst. **53**: 202, 1931. (5) *Reeb, M.:* Gynécologie, p. 137, 1935. (6) *Phaneuf, L. E.:* Am. J. Obst. & Gynec. **21**: 498, 1931. (7) *Phaneuf, L. E.:* Am. J. Surg., New Series **20**: 1, 1933.

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PELVICEPHALOGRAPHY

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THE information obtained from the usual methods of roentgen pelvimetry and fetal cephalometry has been a disappointment to many obstetricians and radiologists. The reasons for this are probably numerous, but mainly it has likely been due to a failure to consider the third dimension. The relationship between the fetal cranium and the birth canal is best visualized by volumetric comparison. The problems in the mechanism of labor cannot be reduced to the simplicity of comparing a fetal skull diameter to a pelvic diameter. Another factor of consequence is the manner of interpretation of roentgenographic data. It must be borne in mind that these data are only additional information which may be utilized in handling a particular case.

It has been emphasized by Thoms[36] and others [33] that external pelvimetry has only a relative value in determining the internal pelvic diameters. Since the birth canal has a direct relationship to the internal pelvic diameters, it is necessary to measure it to know its volume capacity. It is seldom possible by external means to obtain any definite idea of the mass volume of the fetal skull. Therefore, a roentgenographic method which will measure the three dimensional size of the fetal skull and the birth canal should be of aid to the obstetrician.

The author has described such a method which requires only two exposures and does not require any measurements of the patient.[1-3] All of the data are obtained from roentgenograms in the anteroposterior view with the patient in supine position and lateral view with the patient in lateral recumbent position. If preferred, the exposures may be made with the patient standing. Also, by one additional exposure in the anteroposterior view, the films may be examined stereoscopically. The accuracy of the method has been within 5 per cent error for linear measurements and 10 per cent for volumetric estimations. All types of presentations are measurable and the examination may be done with accuracy from the thirtieth week of gestation. In breech presentations additional exposures are, of course, necessary to measure the fetal skull.

The volume of the fetal cranial skull is determined by measuring the circumference of the film images. The mean circumference measurements of a spheroid can be used to calculate its volume (Table I). The circumference measurement eliminates error due to oblique positions of skull diameters in relation to the film and makes it possible to measure all cases. The magnification of the film image is corrected by a calculator

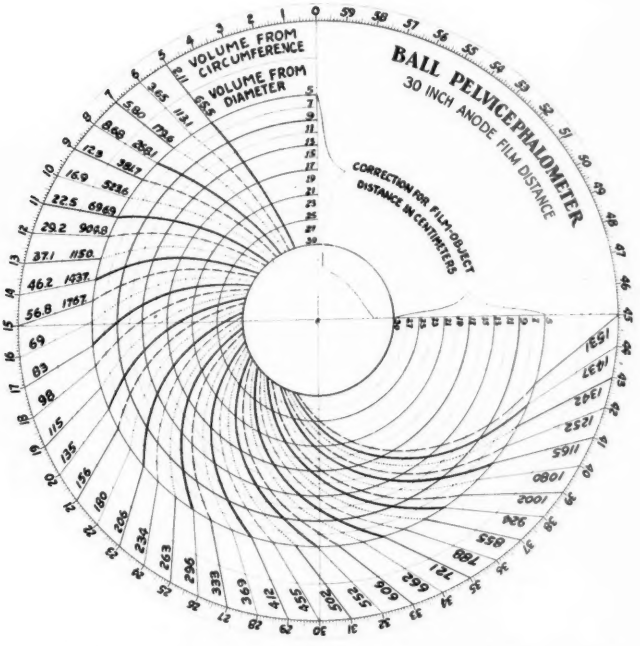

Fig. 1.—A chart for the correction of two variables, which is the dial of the pelvicephalometer.

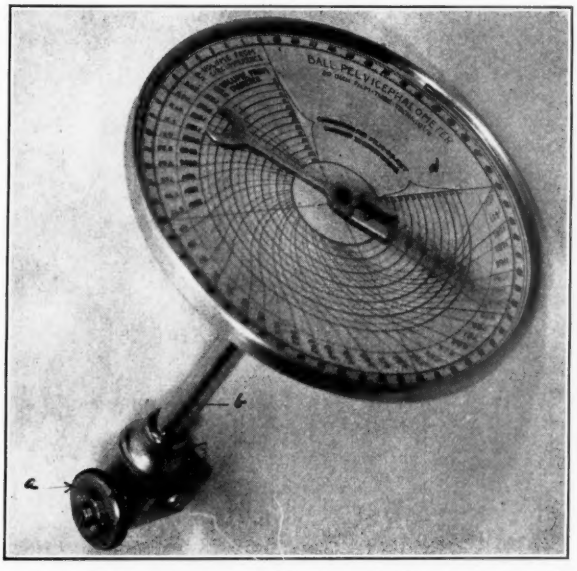

Fig. 2.—The pelvicephalometer. A calibrated wheel (*a*) is traced over the perimeter of the skull image. A shaft inside casing (*b*) is connected with pointer (*c*) which travels over correction chart (*d*).

(correction chart) (Fig. 1), thereby eliminating any mathematical computation. To conveniently obtain measurements, a correction chart was mounted on a dial and the pointer geared to a calibrated contact wheel similar to a map measure, Fig. 2. Two tables showing the volume of a sphere from a circumference measurement (Table I) and volume from a diameter measurement (Table II) are placed on the calculator

TABLE I. SHOWING THE VOLUME OF A SPHERE FROM CIRCUMFERENCE MEASUREMENT

CIRCUMFERENCE	VOLUME	CIRCUMFERENCE	VOLUME
15.0 cm.	56.8 c.c.	33.0 cm.	606.0 c.c.
15.5 cm.	62.8 c.c.	33.5 cm.	636.0 c.c.
16.0 cm.	69.0 c.c.	34.0 cm.	662.0 c.c.
16.5 cm.	75.7 c.c.	34.5 cm.	693.0 c.c.
17.0 cm.	83.0 c.c.	35.0 cm.	721.0 c.c.
17.5 cm.	90.5 c.c.	35.5 cm.	755.0 c.c.
18.0 cm.	98.0 c.c.	36.0 cm.	788.0 c.c.
18.5 cm.	106.5 c.c.	36.5 cm.	820.0 c.c.
19.0 cm.	115.4 c.c.	37.0 cm.	855.0 c.c.
19.5 cm.	125.0 c.c.	37.5 cm.	889.0 c.c.
20.0 cm.	135.0 c.c.	38.0 cm.	924.0 c.c.
20.5 cm.	145.1 c.c.	38.5 cm.	961.0 c.c.
21.0 cm.	156.4 c.c.	39.0 cm.	1,002.0 c.c.
21.5 cm.	168.0 c.c.	39.5 cm.	1,042.0 c.c.
22.0 cm.	180.0 c.c.	40.0 cm.	1,080.0 c.c.
22.5 cm.	192.2 c.c.	40.5 cm.	1,122.0 c.c.
23.0 cm.	205.8 c.c.	41.0 cm.	1,165.0 c.c.
23.5 cm.	218.0 c.c.	41.5 cm.	1,204.0 c.c.
24.0 cm.	233.5 c.c.	42.0 cm.	1,252.0 c.c.
24.5 cm.	248.5 c.c.	42.5 cm.	1,293.0 c.c.
25.0 cm.	263.0 c.c.	43.0 cm.	1,342.0 c.c.
25.5 cm.	280.0 c.c.	43.5 cm.	1,390.0 c.c.
26.0 cm.	296.0 c.c.	44.0 cm.	1,437.0 c.c.
26.5 cm.	314.0 c.c.	44.5 cm.	1,487.0 c.c.
27.0 cm.	333.0 c.c.	45.0 cm.	1,531.0 c.c.
27.5 cm.	350.0 c.c.	45.5 cm.	1,588.0 c.c.
28.0 cm.	369.0 c.c.	46.0 cm.	1,640.0 c.c.
28.5 cm.	389.0 c.c.	46.5 cm.	1,692.0 c.c.
29.0 cm.	412.0 c.c.	47.0 cm.	1,746.0 c.c.
29.5 cm.	433.0 c.c.	47.5 cm.	1,803.0 c.c.
30.0 cm.	455.0 c.c.	48.0 cm.	1,867.0 c.c.
30.5 cm.	478.0 c.c.	48.5 cm.	1,922.0 c.c.
31.0 cm.	502.0 c.c.	49.0 cm.	1,982.0 c.c.
31.5 cm.	524.0 c.c.	49.5 cm.	2,044.0 c.c.
32.0 cm.	552.0 c.c.	50.0 cm.	2,105.0 c.c.
32.5 cm.	578.0 c.c.		

TABLE II. SHOWING THE VOLUME OF A SPHERE FROM A DIAMETER MEASUREMENT

DIAMETER	VOLUME	DIAMETER	VOLUME
5.0 cm.	65.45 c.c.	10.5 cm.	606.13 c.c.
5.5 cm.	87.11 c.c.	11.0 cm.	696.91 c.c.
6.0 cm.	113.10 c.c.	11.5 cm.	796.33 c.c.
6.5 cm.	143.79 c.c.	12.0 cm.	904.78 c.c.
7.0 cm.	179.59 c.c.	12.5 cm.	1,022.70 c.c.
7.5 cm.	220.89 c.c.	13.0 cm.	1,150.3 c.c.
8.0 cm.	268.08 c.c.	13.5 cm.	1,288.2 c.c.
8.5 cm.	321.56 c.c.	14.0 cm.	1,436.8 c.c.
9.0 cm.	381.70 c.c.	14.5 cm.	1,596.3 c.c.
9.5 cm.	448.92 c.c.	15.0 cm.	1,767.1 c.c.
10.0 cm.	523.60 c.c.		

for quick reference and compactness. To the corrected measurement of the perimeter of the fetal cranial skull, 2 cm. are added to allow for the volume of the scalp.

The fetal skull volume is compared to the volume capacity of two pelvic diameters, the true conjugate and the biischial spine. These diameters are chosen because one of the two will always be the smallest pelvic diameter, except in the true funnel pelvis, and the planes of these diameters are parallel to the film when the exposures are made, thereby eliminating obliquity and error in measurement. The pelvic diameter, as measured on the film, is corrected for its magnification by use of the calculator. The linear measurement of the diameter is then interpolated into volume capacity by reference to Table II. Thus the fetal skull volume can be compared to the volume capacity of both or the smallest pelvic diameter. The ratio of the mass volume of the "passenger" to the volume capacity of the "passage" is then expressed in units of volume, milliliters.

The interpretation of a measured disproportion and how it might interfere with a normal spontaneous delivery is naturally subject to data from a large series of cases. Some observations which have been made will be mentioned. Before doing so, however, it is better to discuss briefly the architecture of the pelvis.

The birth canal of the female pelvis is usually described as being cylindrical or ovoid when the walls are compressed anteroposteriorly or laterally. Pelves have many classifications, the majority of which show a great knowledge of descriptive adjectives. A truly descriptive and workable classification of pelves is that of Caldwell and his associates,[9, 10] which is an excellent presentation of the anatomical variations in the bony female pelvis. Moloy and Swenson have attempted by roentgenographic studies to correlate the type pelves with the mechanism of labor. By whatever classification, including pathologic pelves, it should be remembered that the smallest pelvic diameter is the true conjugate or biischial spine, except in the true funnel pelvis, and that, for delivery, the fetal head must pass through the smallest pelvic diameter. In the platypelloid (flattened) pelvis the biischial spine diameter will measure more than the true conjugate; and, conversely, in the android pelvis the true conjugate is greater than the biischial spine diameter. An important question is whether the transverse diameter of the plane of the pelvic inlet is ever smaller than the biischial spine diameter (bony tumors excepted), or if the anteroposterior diameter of the plane at the level of the biischial spines is ever smaller than the true conjugate diameter. To the first part of the question, the author has not, within the limits of his investigation, found an example of such a case. To the second part, there are possibly examples other than the true funnel pelvis, but such a case would show a marked narrowing of the sacrosciatic notch and a loss of the normal convexity of the sacrum. The

lateral roentgenogram, Fig. 3, shows the relationship of this part of the pelvis. Thus, by volumetric comparison, it is important to consider the convexity of the sacrum and the width of the sacrosciatic notch in marginal size cases.

INTERPRETATION OF VOLUME RATIO

Let us assume that a fetal cranial skull has a mean circumference measurement of 31 cm., representing a volume of 502 ml. or c.c. (Table I). We add 2 cm. to the perimeter to allow for the volume of the scalp and find that the cranial skull plus the scalp measures 606 ml. The true conjugate diameter measures 11 cm. and the biischial spine diameter 9 cm. By referring to Table II, it is seen that a sphere of a diameter

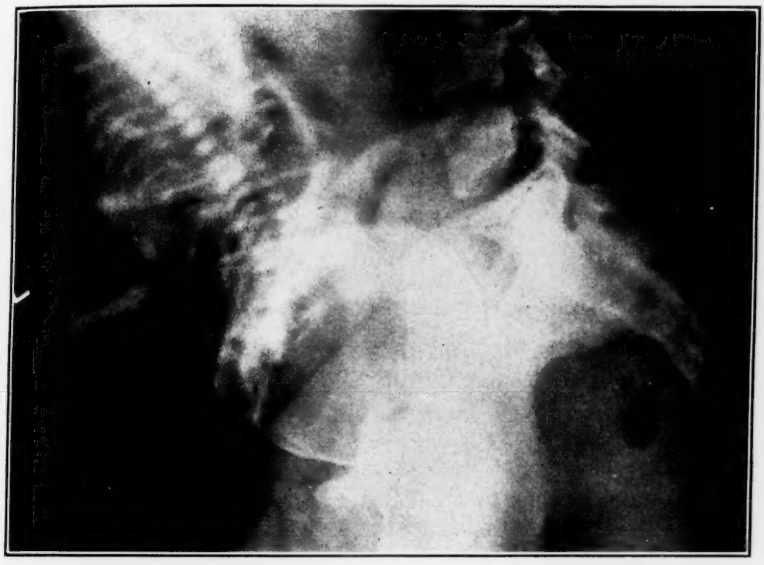

Fig. 3.—Lateral roentgenogram of the female showing a wide sacrosciatic notch and normal convexity of the sacrum.

equal to the true conjugate has a volume of 696 ml. With cephalic presentation in anteroposterior or oblique positions, the space is more than adequate. A sphere equal to the biischial spine diameter has a volume of only 381 ml., while the fetal cranium measures 606 ml., which gives an apparent disproportion of 225 ml. What will be the mechanism by which the cranium passes this pelvic diameter? If the long diameter of the head should attempt to pass in the transverse position, it will not likely get through without a fetal death because approximately 150 ml. has been found by the author to be the maximum limit of head molding without a mortality (cerebral hemorrhage). However with rotation of the head and presentation of the biparietal plane, it is the equivalent of reducing the volume of the cranium by 50 to 100 ml., since the usual difference in occipitofrontal and suboccipitobregmatic circumferences is

from 1 to 2 cm. Assuming in this case only 1 cm. difference in circumference measurements, there is yet 175 ml. more volume of the cranium than volume capacity of the diameter. The scalp volume, surprisingly enough, is 100 ml., and with a 50 per cent compressibility of the scalp, another 50 ml. is reduced from the 175, making 125 ml. that must be taken care of through molding of the head, which is a none too safe margin. However, the pelvic architecture enters into the problem, and with a full curved sacrum and wide sacrosciatic arch, there is available bony space which not only permits easy rotation and adaptation of the optimal cranial diameter but also might allow the major portion of the cranium to pass posterior to the biischial spine diameter. But with a narrow notch, straight type of sacrum and small posterior pelvic capacity, the biischial spine diameter should be large enough to permit the cranium to pass it within safe limits of molding to prevent a fetal mortality. From the series of cases examined it has been found that an unengaged fetal head which measures 150 ml. greater than the volume capacity of the true conjugate diameter is a true disproportion and, with few exceptions, will result in a fetal mortality if submitted to labor. If the biischial spine diameter should be unusually large, suggesting a very wide transverse diameter of the inlet, there is the mechanical possibility of a transverse engagement of the head which would materially lessen the molding necessary to pass the superior strait, a fairly easy spontaneous delivery would be the result. It is, of course, not necessary to emphasize that the above considerations are based upon volumetric comparison and the other factors such as uterine force, etc., are to be considered.

PELVIC CLASSIFICATION WITH TYPES OF PRESENTATION

A classification of pelves based upon the measurement of the true conjugate and biischial spine diameters has been used by the author for convenience. The true conjugate is made the numerator and the biischial spine the denominator of a fraction. When the measurements are within 5 mm., it is called a *one* pelvis because of the close proximity to unity. If the numerator is greater than 0.5 cm., it is called a *one-plus* pelvis and conversely a *one-minus* pelvis; i.e., a gynecoid pelvis with the two diameters near the same size is a *one* pelvis, a platypelloid or flat pelvis is a *one-minus,* and an android with large true conjugate and narrow biischial spine diameters is a type *one-plus.* It will be noted that there is a deficiency in this roentgenographic classification, because the width of the sacrosciatic notch and curve of the sacrum has not been described. For this reason, I again emphasize the excellent classification of Caldwell and associates.

It is interesting to tabulate the type pelves racially and as regards presentation. Table III shows the position and presentation of the

native white, and Table IV, the same in the southern negro. This is a tabulation of only 173 cases, and in a larger series, there is a possibility of some change in the figures, but it is probably representative. Table V indicates that there is no marked racial difference in fetal presentation, although Tables III and IV show considerable variation in type pelves.

VOLUME INCREASE OF FETAL CRANIUM

The absolute rate of increase in volume of the fetal cranium in utero is represented in Fig. 4. The curve is a composite of a series of cases

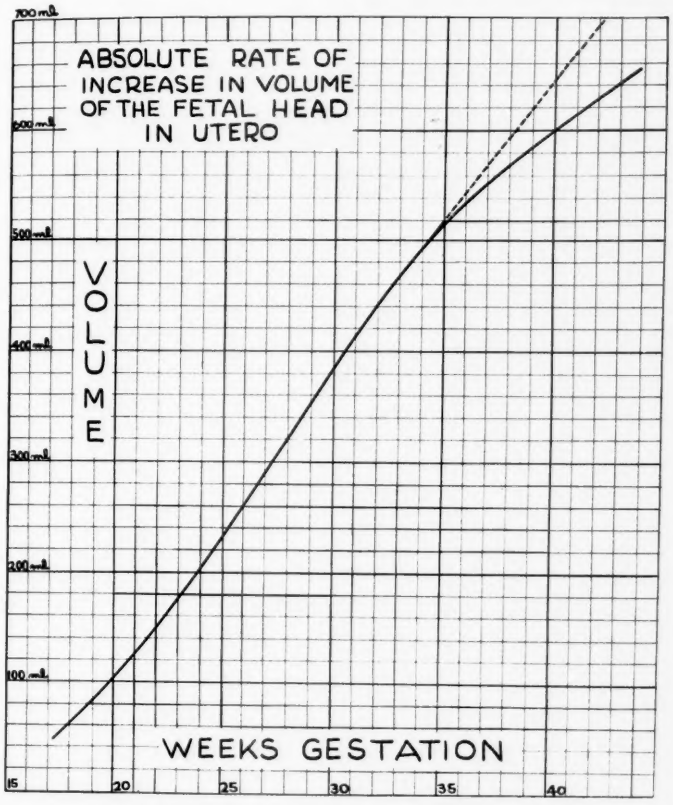

Fig. 4.—The absolute rate of increase in volume of the fetal cranium in utero as obtained from roentgenographic data. The dotted line represents the unengaged head.

examined radiographically at intervals of two to four weeks during gestation. It can be used to estimate the size of the fetal cranium at any period subsequent to the roentgenographic examination, and if it is found to be a marginal size case the examination can be advantageously repeated during labor. The author hopes this curve will be checked closely for its accuracy. It might be utilized to determine fetal death when there have been previous roentgenograms.

TABLE III. THE INCIDENCE OF TYPE PELVES WITH POSITION AND PRESENTATION OF THE FETUS IN THE NATIVE SOUTHERN WHITE

POSITION AND PRESENTATION	TYPE PELVES WHITE			TOTAL
	1	1–	1+	
Breech	3.0	0.0	4.0	7.0
Transverse	0.0	1.0	0.0	1.0
L. O. A.	11.0	9.0	18.0	38.0
L. O. P.	2.0	2.5	3.0	7.5
L. O. T.	6.5	1.5	4.0	12.0
R. O. A.	3.0	1.0	4.5	8.5
R. O. P.	3.0	2.0	9.0	14.0
R. O. T.	5.5	1.0	5.5	12.0
Total	34.0	18.0	48.0	100.0

TABLE IV. THE INCIDENCE OF TYPE PELVES WITH POSITION AND PRESENTATION OF THE FETUS IN THE SOUTHERN NEGRO

POSITION AND PRESENTATION	TYPE PELVES COLORED			TOTAL
	1	1–	1+	
Breech	2.0	0.0	4.5	6.5
Transverse	0.0	0.0	0.0	0.0
L. O. A.	14.0	14.0	6.5	34.5
L. O. P.	8.5	0.0	0.0	8.5
L. O. T.	2.5	0.0	2.5	5.0
R. O. A.	4.5	4.5	4.5	13.5
R. O. P.	12.0	2.0	0.0	14.0
R. O. T.	6.5	4.5	4.5	15.5
L. M. T.	0.0	0.0	2.5	2.5
Total	50.0	25.0	25.0	100.0

TABLE V. A RACIAL COMPARISON OF THE FREQUENCY OF OCCIPITOPOSTERIOR, ANTERIOR AND TRANSVERSE IN PRIMIPARA AND MULTIPARA

POSITION AND PRESENTATION	WHITE		TOTAL	COLORED		TOTAL
	PRIMIPARAS	MULTIPARAS		PRIMIPARAS	MULTIPARAS	
Occipitoposterior	15.0	8.0	23.0	14.5	10.5	25.0
Occipitoanterior	26.0	25.0	51.0	29.0	21.0	50.0
Occipitotransverse	9.5	11.0	20.5	10.5	6.5	17.0
Breech	1.5	4.0	5.5	4.0	2.0	6.0
L. M. T.	0.0	0.0	0.0	0.0	2.0	2.0
Total	52.0	48.0	100.0	58.0	42.0	100.0

SUMMARY

Attention is called to a roentgenographic method of pelvimetry and fetal cephalometry which measures the volume ratio between the fetal cranium and pelvic diameters.

It is desired to emphasize that the roentgenographic data are accessory aid to the obstetrician who will think in terms of the third dimension, and that the mechanism of labor involves a volumetric consideration rather than linear measurements.

The importance of the architecture of the pelvis in the mechanism of labor in marginal sizes only is discussed briefly.

The frequency of occurrence of different type pelves with presentation and position of the fetus near term or in labor in the native southern white and colored is tabulated.

The absolute rate of increase in volume of the fetal cranium in utero as obtained from roentgenographic data is presented.

REFERENCES

Ball, Robert P., and Marchbanks, S. S.: Radiology **24:** 77, 1935. *Ball, Robert P.:* Radiog. & Clin. Photog. **11:** 11, 1935. *Ball, Robert P.:* Surg. Gynec. Obst. **62:** 798, 1936. *Barnes, J. M.:* Am. J. Roentgenol. **32:** 333, 1934. *Bell, J. W.:* Am. J. Obst. & Gynec. **2:** 616, 1921. *Berkeley, C.:* J. Obst. & Gynec. Brit. Emp. **41:** 402, 1934. *Buchner, Edward F., Jr.:* J. Tenn. State M. A. **28:** 30, 1935. *Buckner, D.:* Radiology **23:** 107, 1935. *Caldwell, W. E., and Moloy, H. C.:* Am. J. Obst. & Gynec. **26:** 479, 1933. *Caldwell, W. E., Moloy, H. C., and D'Esopo, D. Anthony:* Am. J. Obst. & Gynec. **28:** 824, 1934. *Chamberlain, W. E., and Newell, R. R.:* Am. J. Roentgenol. **8:** 272, 1921. *Clifford, Stewart H.:* Surg. Gynec. Obst. **58:** 727, 1934. *Cornell, Edward Lyman:* Surg. Gynec. Obst. **53:** 707, 1931. *Davidson, J. M.:* Localization by X-Rays and Stereoscopy, Paul H. Hoeber, Inc., 1916. *Dorland, W. A. N.:* Radiology **3:** 10, 1924. *Gardiner, John P.:* J. A. M. A. **86:** 161, 1926. *Hanson, S.:* Am. J. Obst. & Gynec. **28:** 609, 1934. *Hodges, Paul C., and Ledoux, Alfred C.:* Am. J. Roentgenol. **27:** 83, 1932. *Horner, D. A.:* Surg. Gynec. Obst. **35:** 67, 1922. *Jacobs, J. B.:* South. M. J. **22:** 321, 1929. *Jarcho, J.:* Am. J. Surg. **14:** 419, 1931. *Johnson, Clayton R.:* Am. J. Surg. **8:** 151, 1930. *McKendrick, A.:* Arch. Roentg. Ray **17:** 15, 1913. *MacKenzie, W. R.:* Brit. M. J. **2:** 975, 1923. *Manges, W. F.:* Am. Quart. Roentgenol. **3:** 41, 1911. *Manges, W. F.:* Am. J. Obst. **65:** 622, 1912. *Matthews, H. B.:* Am. J. Obst. & Gynec. **20:** 612, 1930. *Moloy, H. C.:* Am. J. Roentgenol. **30:** 111, 1933. *Murphy, Douglas P.:* Radiology **16:** 770, 1931. *Orley, A.:* Brit. J. Radiol. **6:** 345, 1933. *Pfahler, G. E.:* Am. Quart. Roentgenol. **1:** 23, 1906-1907. *Pieri, R. J.:* Surg. Gynec. Obst. **59:** 891, 1934. *Roberts, R. E.:* Brit. J. Radiol. **32:** 11, 1927. *Stude, W. C.:* Illinois M. J. **66:** 171, 1934. *Thoms, H.:* Surg. Gynec. Obst. **52:** 963, 1931. *Thoms, H.:* Am. J. Obst. & Gynec. **27:** 573, 1933. *Thoms, H.:* Surg. Gynec. Obst. **60:** 680, 1935. *Van Allen, Harvey W.:* Am. J. Roentgenol. **3:** 367, 1916. *Walton, Henry J.:* Am. J. Roentgenol. **25:** 758, 1931. *Williams, J. T.:* Am. J. Obst. & Gynec. **3:** 345, 1922.

Celentano, Pasquale: Is There a Primary Krukenberg Tumor? Arch. di ostet. e. ginec. **42:** 731, 1935.

A woman twenty-four years of age complained of enlargement of the lower abdomen, having no gastric symptoms. Both ovaries and the uterus were removed. The right ovary was the size of the head of a full-term fetus; the left the size of a hen's egg. Microscopic examination showed this to be a Krukenberg tumor.

Convalescence was normal, and no gastric symptoms appeared for about seven months after operation. Four months later she died of a gastric carcinoma. Since there were no gastric symptoms until seven months after operation, might this not be a metastasis from the ovary to the gastrointestinal tract?

JAMES W. PIERCE.

Maggi, Nicolo: Bilateral Sarcoma of the Ovaries, Folia gynaec-demograph. **32:** 4, 1935.

The author describes a case of giant round cell tumor involving both ovaries in a woman thirty-two years old. A discussion of the differential diagnosis between the other common tumors of the ovaries follows. He also refers briefly to tumors of connective tissue origin.

MARIO CASTALLO

HEREDITY AS THE CAUSE OF CONGENITAL MALFORMATIONS

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FROM early times, mankind has sought in the environment the explanation for congenital malformations. The explanations have covered a wide range of possibilities.

An explanation has been advanced recently by Petersen,[4, 5] who claims that changes in the barometric pressure at the time of conception are responsible for malformations.

Petersen states that there is a geographic variation in the appearance of malformations, those areas which are the centers of storm disturbances, or in storm tracks, having the highest number of malformations. In a later paper, he claims that there is also a seasonal variation in the appearance of malformations, more malformed children being conceived in March and April than should be on the basis of expectation, and fewer in July, August, and September than would be expected. He found April and March to have the greatest variation in barometric pressure in the region from which he obtained his data, namely, Chicago.

Murphy,[6] investigating the records for Philadelphia, found that the number of normal conceptions was higher in the late winter and early spring months than at other times, and that the proportion of malformations which were conceived during June, July, and August was disproportionately high; thus they were very low at the time that Petersen found them highest and vice versa. He concluded that there was no evidence, as far as Philadelphia was concerned, that alterations in barometric pressure had any causal relationship to the production of malformations. The barometric pressure in Philadelphia had varied more in January in the five years for which he investigated the conception times than it had in the other months. Dittrich[7] found unduly high proportions of conceptions of malformed individuals in March and August, which he attributed to changes in the ultraviolet light.

It seemed rather unreasonable to conceive of malformations being caused by variations in barometric pressure, inasmuch as the ova, at least, develop in a follicle surrounded by fluid and so are immune from barometric changes. Moreover the barometric changes occurring normally are relatively slight, and as Murphy points out, rather gradual, so that it does not appear reasonable to expect that such an influence as barometric pressure would alter the course of development. Moreover, since not all children conceived in these months exhibit malformations, there must be some individual differences in the susceptibility to variations in pressure, even if that be the correct explanation. The tendency for malformations to occur in more than one child in the family, in a fair proportion of cases, would lead one to think that some inherent quality in that family was mainly responsible for the defects.

MATERIAL USED

Some years ago, I collected a large series of malformations from medical literature, most of them of the bizarre type which were obvious on inspection alone. A few which were internal defects were from cases in which the diagnosis of the malformation had been verified at operation or autopsy. This series was collected to determine the correctness of Still's[8] statement that malformations occurred with undue frequency in first pregnancies, and were due to Nature's inexperience in producing children in that particular union. As Nature became more adept, he said, malformations grew less. This idea was shown to be erroneous (Macklin[2, 3]), the first born being affected in proportion only to their number in the population. In one paper[2] is the bibliography of most of the cases which are used in this study. These references will not be duplicated here because of their length.

Conception Times.—In 256 instances, the date of the last period was mentioned, or the date of birth and the duration of the pregnancy were given. Those cases in which date of birth was given without data as to the date of the last period or the duration of the pregnancy were discarded. The months of conception for these 256 malformed individuals are shown in Table I, and although it is true that in April there were 27 conceptions, there were also 27 in February and July. The five months from September to January inclusive have the lowest number of conceptions, ranging from 14 to 18. It was impossible to attempt any correlation between barometric pressures and conception times in this series, for they were taken from records which covered a long period of years, and a wide range of geographic location. I doubt whether the high incidence of conception in February, April, and July, or the low incidence in the autumn and early winter months has any significance.

TABLE I

MONTH OF CONCEPTION	NO. OF CONCEPTIONS	PERCENTAGE
January	18	7.03
February	27	10.54
March	21	8.22
April	27	10.54
May	24	9.38
June	22	8.61
July	27	10.54
August	25	9.72
September	16	6.24
October	18	7.03
November	14	5.51
December	17	6.64
Total	256	100.00

Heredity as the Cause of Malformations.—In going over the data, two points were brought out which supported both the idea that external causes played a very subsidiary rôle, if any, in the production of

malformations, and that heredity was the important and determining factor. These two points were: (1) the occurrence of malformations in monovular and binovular twins, and (2) the fairly frequent occurrence of the same malformation, or of similar malformations in two or more children in the family. These two points will be discussed in detail, in order to give evidence in support of the idea that heredity is the causal factor.

Incidence of Malformations in Twins.—There are two types of twins: (1) those arising from two eggs, in which the sex may or may not be the same, and in which the heredity of any single trait may or may not be the same, but in which the total heredity is always different. They resemble each other no more nor less than siblings in a family, which are born at different times. (2) There are monovular twins, which are always of the same sex, and in whom the total heredity is as nearly identical as two individuals can be identical. If some cause, operating before birth, such as alteration in barometric pressure, or being the first in the family, or inadequate diet, etc., be responsible for malformations, then whenever twins are born with one showing a defect, *both twins*, whether they be monovular or binovular, should be affected. If the cause of the defect be a matter of heredity in the germ cells, then monovular twins should be alike, either both normal or both defective; but binovular twins might be different or they might be similar.

Among *binovular twins* we should expect to find one pair of like-sexed twins for every pair of mixed twins, since they occur, on the basis of chance, in the ratio of one pair of male twins to one pair of female twins to two pairs of twins of both sexes. Twins are really born in the ratio of one pair of male twins to one pair of female twins to one pair of twins of both sexes. The excess of like-sexed twins is due to the fact that identical or monovular twins are always of the same sex, and increase the number of like-sexed twins. Now, as just stated, if environmental causes be responsible for defects, then we should always find both twins defective, or both twins normal; there should never be any instances of twins where one is normal and the other affected. If, on the other hand, heredity is the cause, then we should find monovular twins always alike, with both normal or both affected; but in the case of binovular twins they might be both normal, both affected, or one normal and one affected. Investigation of malformations in twins should therefore prove fruitful for ascertaining the relative rôles of environment and heredity as the cause of the defects.

One more point should be brought out. If we do find instances in which one of a pair of twins is normal, while the other is affected, such cases should be all binovular, and if the series is large enough, we should expect to find one pair of male twins to one pair of female twins to two pairs of mixed twins. On the other hand, in those instances

in which *both* twins are affected, we should find not only those cases of binovular twins of like and mixed sex in which both were affected, but we should find *all* the cases of monovular twins, for if one is affected, both are; and moreover since they are always of the same sex, we should find a great preponderance of like-sexed twins in the group. The addition of the two groups, those with but one affected and those with both affected, should give the ratio of 1:1:1 which is found in twins in general.

Let us look at the twins which were found in the records investigated. There were 1,420 cases of malformations in the data used. In these there were 55 pairs of twins where one only was affected, and 33 pairs of twins where both were affected. The very fact that we have 55 pairs of twins with one only affected indicates that external factors are probably not responsible for the defects. Of the 55 cases, 15 did not give any data as to the sex of both twins, although 5 of the 15 cases were definitely stated to be binovular. In the 40 instances in which the sex of both twins was given, and but one was affected, there were 9 pairs of male twins, 10 pairs of female twins, and 21 pairs of mixed twins. This is a very close approximation to the 1:1 ratio of like-sexed to mixed twins expected in a group of binovular twins. As was stated above, if heredity is the explanation of malformations, then all twins should be of the binovular type when but one is affected. The data, furnished by the group with but one affected, support strongly the idea that heredity is the cause, and offer no support for the idea that an external factor such as barometric pressure is responsible for the malformations.

Let us look at the information yielded from the group of twins where *both are affected.* There were 33 such pairs of twins. In the case of one pair, both were affected, each had a different malformation, and the sex of the twins was not given. In the 32 instances in which sex was given, both twins had the same defect in every case. There were 15 pairs of male twins, 13 pairs of female twins, and 4 pairs of mixed twins. This is about a 4:3:1 ratio, due to the great predominance of the twins of like sex. Now it might be argued that in this group, barometric pressure was acting equally on both twins, and so this group would support the theory of Petersen. It does not support it however, due to the peculiar sex distribution among these twins. If barometric changes were the explanation, we should find the ratio of 1:1:1 that is found among twins in general. That ratio is altered, because we have concentrated in this group all the monovular twins where the sex must be the same in both, plus the binovular twins where the sex may or may not be the same.

We can determine with some accuracy by two methods how many of these twins should be monovular, and the two results should be in fair agreement. In the first group of twins there were 21 pairs of

mixed twins. Therefore there should have been 42 pairs of like-sexed twins, if this group was representative of twins in general. There were only 19 pairs of like-sexed twins, which meant that approximately 23 pairs of monovular twins were excluded from this group, and should be found as an excess in the group where both twins are affected. In the second group of twins, there were 4 pairs of mixed twins, and so there should have been 4 pairs of binovular twins of like sex, with both affected to correspond to these. There were actually 28 pairs of like-sexed twins, which gives us 24 pairs which were probably monovular. Thus from the first series we see that there should be 23 pairs of monovular twins in the second group, and analyzing the second group, we see that there should be approximately 24; an agreement so close as to be almost identical. Adding the two groups together we have 24 pairs of male twins to 23 pairs of female twins to 25 pairs of mixed twins, again an almost ideal approximation to the 1:1:1 ratio found among twins in general.

That the like-sexed twins are concentrated in the group where *both* are affected; and the ratio expected of males, females, and mixed pairs for binovular twins found where but one is affected, is very good evidence that the malformations in question are not determined by environmental causes but by inherited defects in the germ plasm.

One word must be said here as to joined twins and amorphous twins. Joined twins are necessarily of the same sex, and frequently the only malformation they exhibit is that brought about by their fusion. They were omitted, since they would have unduly weighted the group of twins with both malformed and both of the same sex. Amorphous twins, such as headless or bodyless twins, cases of acardiacus, etc., were omitted. When sex is distinguishable, such a twin and the normal twin are always of the same sex, the two having arisen through the division of a single fertilized zygote into two components, one with a complete set of determiners for normal development, the other with such an incomplete set of determiners as to prohibit development entirely, were it not for the collateral circulation from the normal twin which keeps the other shapeless mass alive. Here although we do have a normal child and an abnormal mass arising from the same egg, they cannot be added to this series, since the amorphous masses cannot properly be called an individual, but are incomplete fragments of human tissue, often without any trace of sex at all.

Incidence of Malformations in Several Siblings.—The evidence from the data furnished by the twins is in favor then of the interpretation that these malformations which we have been discussing, such as spina bifida, anencephaly, exomphalos, lack of arms or legs, atresia of the esophagus, duodenum, imperforate anus, etc., are hereditary. There is a second point which is in favor of this interpretation. If these defects

in development are hereditary, that is, are dependent upon factors resident in the germ plasm, then we should expect to find some families in which more than one child is affected, although we would expect the number of such families to be in the minority. The 1,420 cases were investigated from that standpoint. In 295 instances, the affected child was the first and only child in the family, hence there was no opportunity for a second one to be affected at the time the record was written. Of the remaining 1,125 cases, 311 had records of other children in the family showing a congenital malformation. This was an incidence of siblings affected in 27.6 per cent of the cases. There were 78 cases where 2 in the family were affected; 26 cases where 3 in the family were affected; 15 cases where 4 were defective; 1 where there were 5; and 2 where there were 6 malformed infants.

In the majority of instances, the type of malformation was the same in the affected siblings; in some it was different. Thus in 16 of the 78 families where 2 children were malformed, the type of malformation was different; in 62 families it was the same. In 6 families of the 26 where 3 were affected, the type of malformation was different; and in 20 it was the same. One out of 15 families where 4 were affected had 3 types of malformations, and 1 of the 2 families with 6 affected had different conditions affecting the various members. Sometimes the malformations which were listed as different were in reality due to the same process, but occurring in different sites in the body. Thus one child would have spina bifida in the lumbar region, while a second one in the family would have an encephalocele; or one child would show atresia of the duodenum, while another would be born with imperforate anus.

Petersen's idea concerning the effects of barometric pressure upon the products of conception could of course be put to experimental test. If the explanation holds good for human embryos, it should hold equally for animal embryos. Animals could be put into a sealed chamber in which the barometric pressure could be altered at will. The effect on the progeny could then be studied. Before such an experiment was carried out, however, every animal should be genetically controlled to see whether it produces malformations spontaneously. Thus each male and each female should be bred several times to an unrelated mate, and several times to a related mate, and records carefully kept of all the relationships and the results. Then unrelated males and females, who even when bred with their own litter mates, have produced no malformations, should be bred under the altered barometric pressures, and under normal conditions. Should the number of malformations be considerably greater under the altered pressures, when the same parents show no malformed offspring under normal pressures, we might be led to conclude that altered pressure at the time of conception was a predisposing factor to the production of malformations. Experiments which are de-

signed to test this or other ideas such as malformations caused by unbalanced diets, etc., are worthless unless the genetic aspect of the experiment is rigidly controlled.

It is true that malformations can be produced experimentally in forms like fish by altering the temperature, the chemical constitution of the environment, the oxygen available, and that one cannot claim that such malformations are inherited in these forms. One might as well argue, however, that because one can produce diabetes by removing the pancreas, that all cases of diabetes are due to a complete absence of the pancreas. It is true that one can produce malformations in the mammalian forms by irradiation of the ovary before conception takes place, but no one would be rash enough to claim that malformations which have been known since the beginning of man's history have been due to irradiated ovaries. Moreover, such malformations as Bagg[1] has produced by this method have been shown to be due to a disturbance of the chromosomes by the irradiation, and hence of the hereditary constitution of the animal, for without further experimentation these malformed mice, which have been produced through irradiation of the egg from which they came, have passed on the defect through numerous generations of their descendants.

SUMMARY

A group of 1,420 cases of congenital malformations, either evident externally, or shown by operation or autopsy, were investigated. Of these, 256 gave either the date of the last period, or the birth date of the child, with a statement as to the duration of pregnancy, from which data the month of the conception could be determined with fair accuracy. No significance could be attached in this series to the possible barometric disturbances as a possible cause of malformations.

In the 1,420 cases of malformations were found 40 cases of twins, with one twin malformed; and 32 cases of twins where both twins were malformed, and the sex of the twins was mentioned. The sex distribution in these two groups of twins showed that there was a concentration of binovular twins whose heredity need not be identical, in the "one-twin-malformed group." There was a concentration of like-sexed twins, most of them monovular in the "two-twins-malformed" group. This strongly suggests that hereditary causes are responsible for congenital malformations.

In this group of 1,420 cases, there were 1,125 which occurred in families which had more than one child. There were 311 cases, or 27.6 per cent of these, which were in families where two or more children were malformed. In 60 of the 311 cases, the malformations were not identical in the various members of the family; in the remaining 251 or 80 per cent of the cases, the malformations were identical. This again strongly suggests that the malformation is hereditary in nature. When

there is such a wide variety of malformations to be exhibited, the fact that in 80 per cent of the cases where two or more are malformed in the family, the type of defect is the same in the different affected members, indicates some cause more deep seated than chance variation in barometric pressure.

Inherent defects in the determiners for development are responsible for the vast majority of congenital malformations in man.

I wish to express my appreciation to Dr. Charles C. Macklin, who suggested this study, for his continued support of my studies on the rôle of inheritance in the etiology of disease.

REFERENCES

(1) *Bagg, H. J.:* Proc. Soc. Exper. Biol. & Med. **22**: 271, 1925. (2) *Macklin, M. T.:* Human Biol. **1**: 382, 1929. (3) *Idem:* Lancet **1**: 971, 1929. (4) *Petersen, W. F.:* Am. J. Obst. & Gynec. **28**: 70, 1934. (5) *Idem:* **28**: 443, 1934. (6) *Murphy, D. P.:* Ibid. **31**: 106, 1936. (7) *Dittrich, R. J.:* Human Biol. **1**: 278, 1929. (8) *Still, G. F.:* Lancet **2**: 795 and 853, 1927.

INTRATHECAL INJECTION OF A SOLUTION OF ALCOHOL FOR INTRACTABLE PAIN IN THE PELVIS AND LOWER EXTREMITIES

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THE problem of controlling pain in inoperable malignancies has always been discouraging and because of our helplessness these unfortunate patients are greatly neglected.

It is the purpose of this report to record a method for the relief of intractable pain in the pelvis and lower extremities, and to present the results of its use in ten cases of pelvic carcinoma with involvement of the lumbosacral plexus. The method although not original in the main is somewhat of a departure from that used by others.

TECHNIC

With the patient lying on the least affected side, a spinal puncture needle is introduced in the usual manner between the second and third lumbar vertebrae. Ten cubic centimeters of spinal fluid is withdrawn and discarded. Ten cubic centimeters of a 5 to 7.5 per cent solution of sterile absolute alcohol and triple distilled water is then injected rather rapidly into the spinal canal. The patient is immediately placed flat on the back and required to remain in that position for four hours.

The materials required for the injection are the following: Three medicine glasses; two 10 c.c. syringes; a tuberculin syringe; a 2 c.c. syringe and a hypodermic needle; a small gauge spinal puncture needle with a short bevel; 0.5 to 0.75 c.c. of a sterile absolute alcohol; 9.5 c.c. of sterile triple distilled water; and one small ampule of 1 per cent novocaine.

In this series, eight cases of carcinoma of the cervix, one case of carcinoma of the vulva, and one case of carcinoma of the ovary were

treated. All of these patients were on the cancer service of Dr. Cameron Duncan in Kings County Hospital, Brooklyn, New York, and this work was made possible through his kind cooperation. Brief details of these cases are given as an example of the results obtained.

CASE 1.—E. B., aged forty-five, was admitted to Kings County Hospital, with a diagnosis of carcinoma of the cervix with metastases to the spine. During the past eighteen months she had received extensive x-ray and radium therapy. Two months preceding admission a bilateral cordotomy was performed. She was fairly comfortable for one month, following which there was a return of the old type of pain. On admission she complained of severe pain in the abdomen and back radiating down the legs. The left leg was swollen and the patient was generally in poor condition. After using large and frequent doses of morphine for one month the pain could not be controlled. On Dec, 9, 1933, she was given 10 c.c. of a 5 per cent solution of alcohol according to the technic described above. Thirty minutes later the pain in the pelvis and legs was markedly diminished. She complained of a slight weakness in both legs. This was scarcely appreciable since she had weakness and swelling in both legs before the injection. Analgesia was present in both legs and thighs. Slight hyperesthesia was present over both thighs. There was no bladder or rectal incontinence. From that day until the time of her death, three months later, she was almost entirely free from pain in the lower abdomen and legs. The only sedatives that were necessary following the injection were occasional doses of acetyl-salicylic acid and codeine.

CASE 2.—S. H., aged thirty-seven, was admitted to the hospital with a diagnosis of carcinoma of the cervix with widespread pelvic extension. X-ray and radium therapy were instituted shortly after admission. This patient suffered from a great deal of pain in the abdomen and lower extremities, but was still ambulatory. Little palliation of pain was obtained following irradiation. Occasional doses of morphine with mild sedatives were used unsuccessfully for relief. Ten cubic centimeters of a 5 per cent solution of alcohol were injected intrathecally. Two days after the injection this patient had obtained excellent relief of pain, and it was never necessary during the next four and one-half months, until her death, to give her more than an occasional dose of acetyl-salicylic acid and codeine. Immediately following the injection she suffered a very severe headache which lasted for about twelve hours. Slight weakness in the lower extremities was present with diminished patellar reflexes. Hyperesthesia was present as high as the distribution of the ilio-inguinal nerve. There was no bladder or rectal sphincter disturbance. The patient was up and around on the second day after the injection.

CASE 3.—J. K., aged forty, was readmitted to the hospital after having received extensive x-ray and radium therapy on previous admissions. Diagnosis of carcinoma of the cervix with wide extension and metastases to neighboring lymph nodes. The patient was still ambulatory although pain on motion was excruciating. Frequent doses of morphine were necessary for relief. Intrathecal injection with 5 per cent solution of alcohol was done. Maximum relief was obtained on the third day. Only a dull pelvic and lower extremity pain were complained of from that time until her death two months later. Morphine was gradually diminished and she was finally kept comfortable with acetyl-salicylic acid and codeine. Shortly after the injection tendon reflexes were diminished. There was slight motor weakness of the lower extremities with hyperesthesia extending to four fingers above the pubis. Bladder and rectal sphincter action remained normal. This patient continued to be ambulatory until shortly before her death two months later.

CASE 4.—M. W., aged thirty-five, who had received a complete course of x-ray and radium therapy during a previous stay in this hospital, was readmitted. Diagnosis on the first admission was that of a carcinoma of the cervix with extension through the pelvis and metastases to the surrounding lymph nodes. The condition had not appreciably regressed at the time of this admission. She was complaining of intense pain in the abdomen and legs. Since this was one of our first cases, she was given an intraspinal injection of 10 c.c. of only a 2 per cent solution of alcohol. She obtained no relief of pain. Clinically there were no signs of diminished motor function, hyperesthesia, or sphincter disturbances. This patient refused a second injection and the therapy was a failure due to inadequate dosage.

CASE 5.—J. L., aged sixty-three, diagnosis of carcinoma of the vulva with metastases to both inguinal lymph nodes. This patient on a previous admission to the hospital, about eight months ago, had been subjected to an operation for complete vulvectomy. Since the lesion was small, removal of the inguinal lymph nodes was not done, but she received a full course of irradiation over these glands. On her present admission inguinal glands on both sides had become extensively involved. Glands in the left inguinal region had broken down with deep slough down to the femoral vessels. This patient was bedridden and pitiful in her misery. She was given 10 c.c. of a 5 per cent solution of alcohol intrathecally. By the third day she had obtained good analgesia in the lower abdomen and lower extremities. As in all of our cases the patellar reflexes were diminished, and she had slight motor weakness of the lower extremities for about twenty-four hours. Hyperesthesia extended to about the level of the distribution of the eleventh thoracic nerve. This patient had a very violent headache which persisted for eighteen hours and could only be relieved with morphine. Bladder and rectal sphincter action remained normal. Pyramidon and codeine were sufficient to keep her comfortable up to a few days before her death, four and one-half months later, which followed erosion through the femoral vein.

CASE 6.—K. A., aged thirty-four, admitted to the hospital with an advanced carcinoma of the cervix with wide parametrial extension and pelvic metastases. X-ray was begun for palliation. Since her pain was so intense, she was given 10 c.c. of a 5 per cent solution of alcohol intraspinally, and by the fourth day had obtained excellent relief of pain. She showed diminished reflexes and slight weakness. Moderate hyperesthesia was present as high as the level inguinal ligaments. There was no disturbance of the bladder and rectal sphincter action. Relief continued until her death six weeks later.

CASE 7.—N. C., aged thirty-two, admitted to the hospital with a diagnosis of a carcinoma of the cervix with extension into the bases of both broad ligaments, but no evidence of other metastases. Intraspinal injection of 10 c.c. of a 5 per cent solution of alcohol was done, and on the second day, she had obtained good relief of pain. Hyperesthesia, motor weakness, and diminished tendon reflexes in the lower extremities were all present for about twenty-four hours. Bladder and rectal sphincter action continued to be normal. Radium followed by x-ray treatment were instituted. Until her death three and one-half months later, following exsanguinating hemorrhages, she was kept comfortable with acetyl-salicylic acid and codeine.

CASE 8.—C. L., aged forty-four, admitted to the hospital with a diagnosis of carcinoma of the cervix with involvement of the entire pelvis. Patient was in an extremely weakened condition and suffering from unbearable pain. Ten cubic centimeters of a 5 per cent solution of alcohol were given intrathecally. The maximum effect was evident by the second day and good relief of pain was obtained. Motor

weakness and hyperesthesia in both lower extremities with lessened reflex responses were noted. Bladder and rectal sphincter action remained normal. Acetyl-salicylic acid and codeine were all that was necessary to keep her comfortable during the following month. At that time she developed a psychosis and became so violent that it was necessary to administer additional sedatives and to keep her in a strait-jacket until death one month later.

CASE 9.—E. T., aged seventy, admitted with carcinoma of the uterus thought to have originated in the fundus, but now so widespread throughout the pelvis and lower abdomen that the original focus could not be definitely determined. She had received an unknown amount of x-ray therapy about two years previous to admission. This patient was ambulatory and was suffering a great deal from pain in her lower abdomen and legs. She was given 10 c.c. of a 7.5 per cent solution of alcohol intrathecally. By the third day after the injection she had obtained good relief of her pain. No change in the function of her bladder and rectal sphincter was noted. She continued to be ambulatory although for the first twenty-four hours she complained of slight weakness in her legs. Patellar reflexes were diminished. Hyperesthesia was rather marked, and she complained of a sensation of tingling in her lower extremities. She was kept comfortable with pyramidon and codeine until the time of her death two months later.

CASE 10.—C. K., aged fifty-five, admitted to the hospital with a diagnosis of carcinoma of the ovary with generalized abdominal metastases. The patient had had exploratory laparotomy two months previous to this admission, followed by deep x-ray therapy. She was suffering from exquisite pain in the lower abdomen and was unable to obtain any rest. Ten cubic centimeters of a 7.5 per cent alcohol solution was given intrathecally. Examination showed lessened reflexes, moderate motor weakness, and mild hyperesthesia of the lower extremities. There were no bladder or rectal disturbances. Acetyl-salicylic acid and codeine were sufficient for relief of pain until her death one week later.

REVIEW OF LITERATURE

In 1931 Dogliotti[1] reported the first series of more than 40 cases in which alcohol had been given intraspinally for the relief of pain in the lower extremities. In his series he used 0.5 to 1 c.c. of absolute alcohol (undiluted). His needle was inserted between the second and third lumbar vertebrae, and the patient was made to lie on the unaffected side for twenty minutes following the injection. It is interesting to note that he dared to use this therapy in sciaticas, radiculitis, in arthritis deformans, tabetics, femoro-cutaneous neuralgias, perineo-coccygeous pain, intercostal neuralgias, and diabetic neuritis. He suggested at the time the possibilities of its use in pelvic malignancies. Some time later when he was visiting F. C. Yeomans Clinic, he was invited to demonstrate his method on a patient with inoperable carcinoma of the rectum. Subsequently Yeomans[2] reported a series of seven similar cases all with good results. In the past year, Saltzstein,[3] using the method of Dogliotti has reported good results in the relief of pain. His cases included 1 case of carcinoma of the breast, 1 case of carcinoma of the prostate, and 5 cases of carcinoma of the cervix. At about the same time, Stern[4] reported a series of 19 cases of carcinomas, in the majority of which he considered having obtained satisfactory results by the use of Dogliotti's method. Stern gave injections as high as the seventh thoracic interspace, and suggested injections as high as the first thoracic interspace. More recently Greenhill and Schmitz[5] have reported an additional series of 25 patients all with malignancies of the female genital organs. They obtained relief in 24 of the 25 patients treated.

Opinion differs as to the length of time required to get the maximum effect from the drug. Dogliotti reports some cases as taking as long as ten to twenty days. Saltzstein says relief was immediate in all of his cases. Stern, Greenhill, and Schmitz coincide in their findings with Dogliotti. Examination of the patients in this series showed greatest relief on the fourth day after injection.

Reactions are not disturbing. Headaches occur in about 50 per cent of the cases. The incidence may be diminished by forcing the patients to lie flat on their backs for the full four hours. In two cases the headache persisted for twenty-four hours, and sedatives were required for relief. Tendon reflexes are diminished and a slight transient motor weakness, lasting from one to four days, is usually present. Hyperesthesias can be elicited, both superficial and deep, up to the level to which the analgesia has extended. In only one case was this sufficiently marked to cause the patient to complain of pain from the bedclothes touching. This hypersensitivity had disappeared by the second day. Bladder or rectal sphincter disturbance did not occur in any case.

In one case of Dogliotti's series there was retention of urine for forty-eight hours followed by the return of normal sphincter action. Greenhill and Schmitz report one case in which 2 c.c. of absolute alcohol injected intraspinally within a period of two days caused atrophy and anesthesia of the left leg. Stern reports a case in which 30 minims of absolute alcohol caused complete loss of muscle, tendon, and joint sense, and loss of control of the lower limbs, and a second case in which an injection of sixteen minims of absolute alcohol caused sensory bladder paralysis for one week.

Sicard and Byrne[12] believe that sensory fibers are more susceptible to the effect of alcohol than are the motor fibers. Cadwalader claims that both were affected alike. I tend to agree with the latter view.

Since no patient in this series lived longer than four and one-half months, it is impossible to say how much longer the analgesia would have lasted. Other patients reported were kept comfortable for from six to eighteen months.[1, 2] The results to date make this type of treatment appear to be the most efficacious of the many methods that have been tried, and its technic is sufficiently simple to promote its widespread use and determine its true value in a large number of cases.

Brief mention is made of the other methods in use at the present time for the relief of pain in these cases, merely in order to contrast them with this type of therapy. We may divide them into two groups, those in which sedatives are used to dull the appreciation of pain and those in which there is an actual interruption of the nerve pathways either by surgery or by degenerating drugs.

The use of sedatives, principally the opiates, are seldom satisfactory since the increasing tolerance of the patient for the drug makes larger and larger doses finally inadequate for the control of the pain. Frequently we must forego the use of opiates entirely because of disturbing idiosyncrasies to opium derivatives.

In the surgical interruption of the nerve tracts a rhizotomy, peripheral nerve section, cordotomy, or sympathectomy may be performed. However, specialized technic is necessary in these procedures, and they are all attended with some shock in patients who are not considered good operative risks.

In the use of degenerating solutions for destruction of the nerve pathways the more usual operations are paravertebral injections of the peripheral nerves, sacral epidural injections and occasionally attempts are made to do paravertebral injection of the sympathetic ganglia. Failure is much more frequent than is success in these cases because of the difficulty of locating these nerve tissues through four or five inches of muscle and fat. If the injection of a peripheral nerve is correctly done, transmission of all motor and sensory impulses are destroyed. If the area to be relieved of pain is large, this complete anesthesia and motor paralysis will be very disturbing.

COMMENTS AND CONCLUSIONS

1. Although no marked motor or sensory disturbances have been encountered in this series this treatment seems, at present, too radical to recommend in any but incurable cases.

2. Injections in this series were made in the second lumbar interspace or lower. In this region there is no cord, but only cauda equina, and we are also below the extent of the dorsal suspensory ligament of the cord which is believed to prevent free passage of fluid from one side of the spinal canal to the other, but this has never been proved. Injections are made rapidly for the purpose of equal and widespread diffusion of the alcohol solution over the lumbar nerve roots and cauda equina, usually bilateral relief is desired, and this is the method of obtaining it. Alcohol in the spinal canal, even if not barbotaged, diffuses fairly rapidly. Torsion of the spinal canal is not considered necessary in the solution injection method. The analgesia is similar to that produced by small doses of well-barbotaged spinal anesthetic drugs, but since the nerve narcosis with alcohol is more persistent, it is better suited for our purpose.

3. A great deal of pain in the abdomen and lower extremities from pelvic carcinoma is reflex. The wide distribution of the pain with proof of the absence, in many cases, of direct pressure on peripheral roots and trunks, suggests involvement by irritation of the cord segments from which these nerves arise. It is found that the termination in the cord of the sympathetic and sacral autonomic fibers from the diseased area corresponds to the segments of origin of the peripheral nerves involved in the distribution of pain. It is thought that the sympathetic and sacral autonomic fibers making up the hypogastric plexus are not paralyzed by this strength of solution but their conductivity is greatly reduced. The fact that occasional bladder and rectal disturbances are reported favors the belief that a large amount of the benefit derived from this therapy is by its effect on the autonomic nervous system. There is some direct effect on peripheral nerves, since we get hyperesthesias and motor weakness in all areas supplied by the peripheral nerves in the region of injection. Immediate relief of pain is probably due to the direct effect on

peripheral nerve roots, later progressive relief of pain up to the fourth day is due to gradual recovery of the irritated cord segments following diminution of the steady stream of stimuli through the sympathetic and sacral autonomic afferent fibers.

4. A low concentration of alcohol is sufficient to diminish the conductivity of the nerve fibers so that only strong, and repeated impulses will pass through. An initial dose of 10 c.c. of a 5 per cent to 7.5 per cent solution repeated once after four days is considered within the limits of safety.

5. Pain was markedly diminished in all cases except one. In the failure, only a 2 per cent solution was used, which is an inadequate dose, and the patient refused a second injection. The results obtained in this series would indicate that this type of treatment is more successful in selected cases than is paravertebral injection of spinal nerves and sympathetic ganglia, sacral blocks, and occasionally even cordotomy. Complete anesthesia cannot be expected but there is always excellent analgesia. Peripheral pain was poorly relieved in areas supplied by nerve roots originating in the spinal cord above the twelfth thoracic and first lumbar segments.

6. Dogliotti's method seems preferable in cases of unilateral localized involvement and where pain is due to direct pressure on the peripheral nerve trunk.

REFERENCES

(1) *Dogliotti, A. M.:* Presse méd. **39:** 1249, 1931; Rev. neurol. **2:** 485, 1931. (2) *Yeomans, F. C.:* J. A. M. A. **101:** 1141, 1933. (3) *Saltzstein, H. C.:* J. A. M. A. **103:** 242, 1934. (4) *Stern, E. L.:* Am. J. Surg. **25:** 217, 1934. (5) *Greenhill, J. P., and Schmitz, Herbert E.:* J. A. M. A. **105:** 406, 1935. (6) *Sicard and Byrne, J.:* J. Nerv. & Ment. Dis. **53:** 433, 1921. (7) *Condamin, F., and Arnulf, G.:* Rev. de chir., Paris **70:** 635, 1932. (8) *Wright, Samson:* Applied Physiology, New York, 1934, Oxford University Press. (9) *Kuntz, Albert:* Autonomic Nervous System, Philadelphia, 1934, Lea & Febiger. (10) *MacLeod, J. J. R.:* Physiology and Biochemistry, ed. 5, St. Louis, 1926, The C. V. Mosby Co. (11) *Ruth, H. S.:* J. A. M. A. **102:** 419, 1934. (12) *Gilcreest, E. L., and Mullen, T. F.:* S. Clin. North America **11:** 989, 1931. (13) *Alvarez, W. S.:* Am. J. Surg. **14:** 385, 1931. (14) *Dyas, F.:* Surg. Gynec. Obst. **33:** 184, 1921. (15) *Viner, N.:* Canad. M. A. J. **15:** 630, 1925. (16) *Viner, N.:* Canad. M. A. J. **15:** 1136, 1925. (17) *Reichert, F. L.:* Northwest Med. **31:** 554, 1932.

MEDICAL ARTS BUILDING

Roberto, S.: The Presence of Vitamin E in the Blood of Fertile Women, Riv. ital. di ginec. **18:** 105, 1935.

The author, after thorough discussion of the question of vitamin E, refers to the results of his experimental research on the presence of this vitamin in the blood of fertile women. Using the rat for the experiments he states that while the function of reproduction is profoundly impeded in animals placed on a synthetic diet lacking the E factor, it persists unchanged in those in which is administered the same diet with the addition of blood from pregnant women.

In conclusion he infers that in the blood of fertile women there is present a rich source of the E factor.

AUGUST F. DARO.

A STUDY OF THE ACTION OF THE GONADOTROPIC SUBSTANCES PRECIPITATED BY TANNIC ACID

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THE early determination of pregnancy by subjective physical changes and the objective findings is rather unreliable. However, the determination of pregnancy by chemical reactions is relatively much more accurate. Such chemical reactions may be demonstrated by: *first*, color changes;[1-3] *second*, pupillary reactions;[4] or, *third*, the ovarian reaction to the stimulating substance present in body fluids during pregnancy. These ovary-stimulating substances have been reported to be present in the blood, urine, placenta,[5-7] decidua, colostrum,[8] amniotic fluid, and saliva[9, 10] of pregnant women and in milk[8, 11, 12] and the serum of blisters produced by cantharides.[11] They are said to be absent in cerebrospinal fluid[13-16] and gastric juice[9, 15] of pregnant women. In the human, the placenta, blood serum, and urine contain the substance or substances in greatest amounts. The precipitants which have been used either on crude urine or on a partially purified product have included not only such solvents as alcohol and acetone[17-19] but also the following: 1. kieselguhr,[20] 2. ammonium sulphate,[21] 3. tannic acid,[21] 4. phosphotungstic acid,[22, 23] 5. Lloyd's reagent,[11, 24] 6. kaolin,[25] 7. norit,[19, 26, 27] 8. benzoic acid,[27] 9. tungstic acid,[28, 29] 10. uranyl acetate,[30] 11. aluminum hydroxide,[31] 12. phosphomolybdic acid,[23] 13. sodium tungstate,[3] 14. colloidal iron,[21, 22] 15. alundum,[31] 16. tricalcium phosphate,[31] and 17. talc.[31]

Tannic acid has never been used on crude urine.* Dickens[21] tried it on a partially purified solution of the ammonium sulphate precipitate of pregnancy urine and reported that "it caused nearly quantitative precipitation of the activity." We believe that because of its comparative cheapness, tannic acid would serve well in the preparation of the gonadotropic substance from crude urine and other secretions of the body. We have studied its use for this purpose both in urine and in saliva.

EXPERIMENTAL

Urine from women pregnant five to seven months, obtained from the Out-Patient Department of the University Hospital, is acidified to a pH 4 to 5 (spot plate method) with glacial acetic acid, using bromcresol green as the indicator. If the

*After we had completed our work we learned that Hellbaum, Fevold, and Hisaw had reported on the use of tannic acid to concentrate the gonadotropic activity in crude urine in Proc. Soc. Exper. Biol. & Med., p. 1566, June, 1935.

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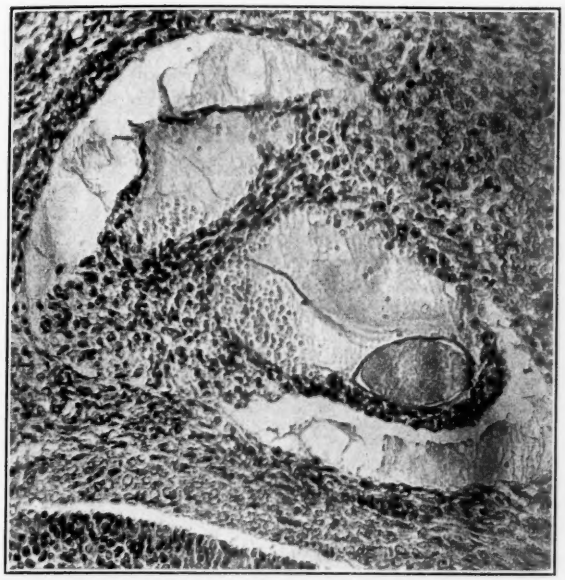

Fig. 1.—Ovary of immature rabbit receiving intravenously (in four equally divided doses at fifteen-minute intervals) the substance precipitated from 240 c.c. of pregnancy urine.

Fig. 2.—Ovary of a mature rabbit killed twenty-two hours after receiving an ammoniacal solution of the substance precipitated by tannic acid from 125 c.c. of urine of pregnancy.

urine is not clear after acidifying, it is centrifuged. One per cent by weight of tannic acid, dissolved in the least amount of water, is added. The heavy gray white precipitate may be centrifuged immediately or stand in the ice box overnight or longer. It is then centrifuged, washed with alcohol and ether, and extracted immediately with a small amount of approximately tenth-normal ammonium hydroxide, or permitted to stand under an alcohol-ether mixture overnight (or longer) and extracted the next day. It was observed that our immature rabbits did not survive the injection of an extract prepared from 25 c.c. or more of pregnancy urine, whereas mature rabbits survived the equivalent of 125 c.c. or more. The earliest changes in immature female rabbits were observed four hours after injection, and consisted of hyperemia of the uterine horns and tubes, injection and interstitial hemorrhage of the ovaries, and degenerative follicular changes. Fig. 1 is a photomicrograph of a paraffin section of the ovary of an immature rabbit, dying four hours after receiving the first of four injections (given at fifteen-minute intervals) of the substance precipitated from 240 c.c. of the urine of pregnancy. It illustrates the changes mentioned above.

Our findings are contrary to the observations of Reinhart and Scott[32] who state that "luteinization of the hemorrhagic follicles in the rabbit ovary begins between the forty-eighth and ninety-sixth hour after injection; and there are then seen partially luteinized hemorrhagic follicles." We found microscopic evidence of luteinization in our mature rabbits which had received the substance precipitated by tannic acid at nineteen to twenty-two hours after the injection; and gross evidence of luteinization and hemorrhage at the end of thirty-six hours. Fig. 2 is a photomicrograph of a paraffin section of the ovary of a mature rabbit killed twenty-two hours after receiving an ammoniacal solution of the substance precipitated by tannic acid from 125 c.c. of urine of pregnancy.

To determine whether 1 per cent by weight of tannic acid was sufficient to insure complete precipitation, the supernatant liquid was tested with more tannic acid. No further precipitation occurred. Furthermore, a white mature female rabbit which received an intravenous injection of 10 c.c. of the supernatant urine showed no gross indication of the pregnancy hormones.

EFFECT OF INTRAVENOUS INJECTION OF THE ALCOHOL-INSOLUBLE FRACTION OF THE AMMONIACAL SOLUTION

The addition of 20 to 30 volumes of 95 per cent ethyl alcohol to each volume of the ammonium hydroxide solution of the substances precipitated by tannic acid from the urine of pregnant women precipitates a dirty white, flocculent, active substance which is soluble in water. Fig. 3 is a photomicrograph of a paraffin section of the ovary of a mature rabbit killed forty-two hours after receiving intravenous injections of an aqueous solution of the substance precipitated by alcohol, from an ammoniacal solution of the active substance obtained from 285 c.c. of urine by precipitation with tannic acid. It shows hemorrhage in a luteinized follicle. Fig. 4 is a photograph of a longitudinal section of the ovary of a mature rabbit killed nineteen hours after receiving an intravenous injection of the alcohol-insoluble fraction (two precipitations) of the ammoniacal solution of the active substance from 68 c.c. of urine. The lutein bodies are very prominent.

Our observations are contrary to those of Elden[33] who states, "The active material, after adsorption and extraction from urine of pregnancy, is not precipitated by alcohol, acetone, or ammonium sulphate"; and Wiesner and Marshall[22] who state, "No active precipitate has been obtained (in two experiments) from an ammoniacal solution of the active substance by the addition of alcohol to a concentration of 90 per cent." A biuret test, made on an aqueous solution of the active substance, prepared as described is negative.[17]

It was observed that an immature rabbit did not survive the injection of material obtained, as described, from more than 135 c.c. of urine of pregnancy; whereas, a mature rabbit tolerated 285 c.c., or more. The earliest gross changes in the mature female rabbit were present at nineteen hours and consisted of the formation of corpora lutea. Later changes included hemorrhage into the luteinizing follicle. This harmonizes with the statements concerning luteinization and hemorrhage in the rabbit, found in Maximow and Bloom *Text-Book of Histology*, second edition.

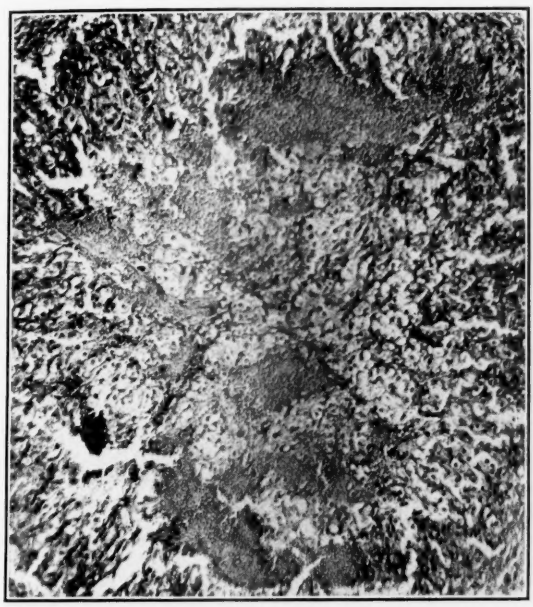

Fig. 3.—Ovary of a mature rabbit killed forty-two hours after intravenous injections of the aqueous solution of the substance precipitated by alcohol, from an ammoniacal solution of the active substance obtained from 285 c.c. of pregnancy urine.

Fig. 4.—Ovary of a mature rabbit killed nineteen hours after receiving intravenously the alcohol insoluble fraction of the ammoniacal solution of the active substance obtained from 68 c.c. of pregnancy urine.

The earliest changes in immature female rabbits were observed three and one-fourth hours after injection and consisted of hyperemia of the uterine horns and tubes, enlargement, injection, and interstitial hemorrhage of the ovaries. Microscopic examination of the liver and kidneys of animals receiving this injection revealed marked changes at the end of seventy-two hours. Dr. L. A. Turley, of the Department of Pathology, points out that in the frozen section of the kidney the

capillaries of the glomeruli are swollen. The tubules contain albuminous débris and the tubule cells show degenerative changes. There are present a few red blood cells, both in the tubules and in the subcapsular space of the glomeruli. Also, in the frozen section, the liver cells show marked degenerative changes. There are a few areas of hemorrhage. The epithelial lining of the bile ducts is swollen. These changes are at present receiving further consideration in our laboratory.

EFFECT OF ORAL ADMINISTRATION

The effect of the enzymes upon the gonad-stimulating substance was studied by Dickens[21] who stated that it "is not rapidly destroyed by trypsin or pepsin though prolonged treatment causes inactivation"; and by Wiesner and Marshall[22] who state definitely that the activity is destroyed by trypsin. The oral administration of the gonadotropic substance has been tried on rats[20, 34] with a variable degree of success.

We administered the extract obtained from 200 c.c. of human pregnancy urine by tannic acid precipitation, extraction with dilute ammonium hydroxide, and reprecipitation with 25 volumes of 95 per cent ethyl alcohol, in an aqueous solution via stomach tube, and seventy-two hours later both gross and microscopic findings were negative for pregnancy.

EFFECT OF INJECTING WHOLE SALIVA INTRAVENOUSLY

Contradictory statements are found concerning the presence of the hormones in saliva. Trancu-Ranier,[9] working with infantile mice, obtained follicle ripening but stated that hemorrhage into the follicle is very weak and seldom seen; and typical lutein bodies are rare. Ofstad,[10] also working with mice, found no gross or microscopic evidence of the presence of the hormones. At the suggestion of Dr. Edward C. Mason, of this department, we have studied the action of the saliva of pregnant women on both mature and immature female rabbits. In one mature rabbit, isolated three months, which received 18 c.c. of saliva intravenously at 3:00 P.M. and was found dead the next morning, we observed microscopically two well-formed corpora lutea. In immature rabbits receiving injections of saliva, no lutein tissue was observed. There were, at the end of thirty-six hours, however, degenerative changes of the granulosa, small amounts of hemorrhage into a few follicles, and an injection of all the vessels. In one immature animal the uterine horns and tubes were injected sixty hours after the initial intravenous injection. All animals, regardless of their age, showed a strong shocklike reaction to the intravenous injection of untreated saliva. Experiments attempting to determine the cause of this condition are being conducted at the present time.

Fig. 5 is a photomicrograph of a paraffin section of the ovary of an immature rabbit, forty-nine hours after the first injection of saliva of a pregnant woman. It shows degenerative changes and hemorrhage in the follicle.

EFFECT OF INTRAVENOUS INJECTION OF THE AMMONIACAL SOLUTION OF THE TANNIC ACID PRECIPITATE OF SALIVA OF PREGNANCY

One mature rabbit which received the extract made from 25 c.c. of saliva showed no positive gross findings at the end of forty-six hours. Microscopically, we observed some indefinite changes of the granulosa and numerous red blood cells in the coagulum of the follicles. In two immature rabbits which received the extracts made from 45 c.c. and 110 c.c., respectively, there were no gross changes at the end of twenty-six and sixty-seven hours; but microscopically, we observed injection

(especially of the thecal vessels), degenerative changes of the granulosal layers and an infiltration of leucocytes and red blood cells into some follicles. Fig. 6 is a

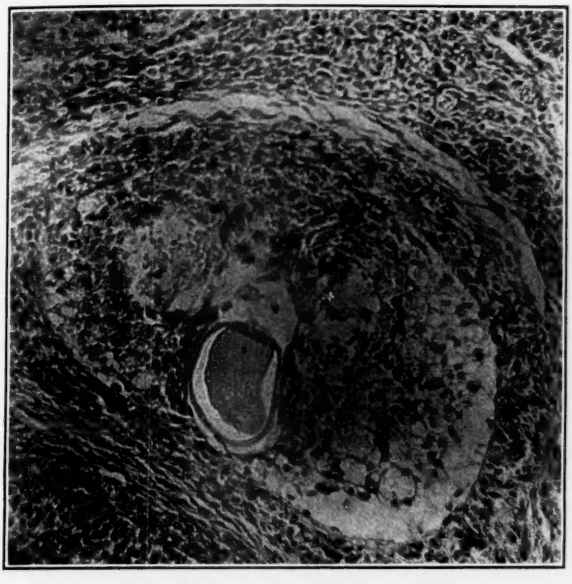

Fig. 5.—Ovary of immature rabbit forty-nine hours after the first injection (of a series totalling 53 c.c.) of whole saliva of pregnant women.

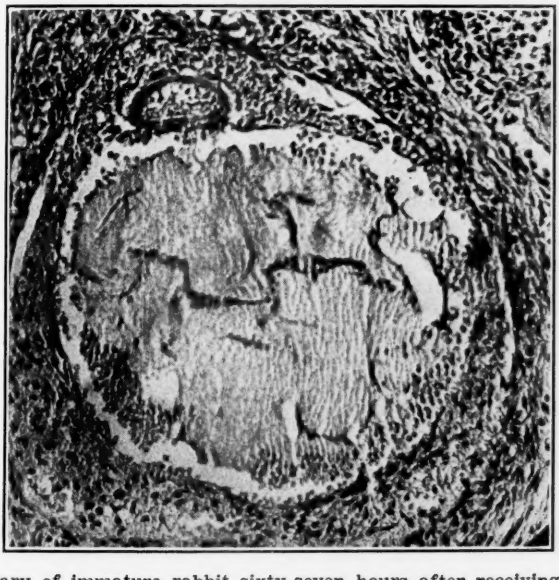

Fig. 6.—Ovary of immature rabbit sixty-seven hours after receiving intravenously the ammoniacal solution of the substance precipitated by tannic acid from 110 c.c. of saliva of pregnant women.

photomicrograph of a paraffin section of the ovary of a rabbit sixty-seven hours after receiving the ammoniacal solution of the substance precipitated from 110 c.c. of saliva of pregnant women, by tannic acid.

DISCUSSION

The difference in the response of mature and immature rabbits both to saliva and to urine indicates the greater sensitivity of the mature animals. It is conceivable that some of the contradictory observations on saliva are due to this fact. The occasional false negative reactions, using urine, may be caused by the use of immature animals; or, at least, insufficient dosage for the immature animal.

King[35] who has made an analysis of 4,515 cases presented by thirty-four authors and involving seven different technics, with minor variations, reports an uncorrected error of 3.9 per cent; of this, 3.3 per cent represent false negatives. Since most of the animals used in these technics were immature, it is conceivable that the large percentage of false negatives may be partially, at least, due to the age factor. Wilson and Corner[36] advocate the use of fully matured female rabbits. They examine the animals sixteen hours after the injection, and their results compare very favorably with the results of other investigators who use immature rabbits but make the examination thirty-six hours after injection. Friedman,[39] in 1929, recommended mature rabbits. Hirsch-Hoffmann,[37] as well as Sar-louis,[38] advocate the use of mature mice.

CONCLUSIONS

1. Tannic acid completely precipitates a gonadotropic substance from crude urine, as evidenced by tests on mature and immature female rabbits. The substance obtained from as little as 15 c.c. of urine gives a strong grossly positive reaction at seventy-two hours in an immature female rabbit. The earliest conclusive change was observed twenty-two hours after injection.

2. Alcohol precipitates an active fraction from the ammoniacal solution. This precipitate produced gross luteinization nineteen hours after injection in a mature rabbit.

3. The earliest postmortem findings were injection of the uterine horns and tubes, and swelling of the ovaries. These findings, however, were not constant.

4. Except for hyperemia and interstitial hemorrhage, the earliest ovarian changes noted were luteinization.

5. Oral administration was ineffective in the dosage given.

6. Crude saliva gave a positive microscopic test in one mature rabbit. No positive gross reactions were noted. Microscopic changes were observed in immature rabbits which received either crude saliva or an extract prepared by tannic acid precipitation; but these changes were not conclusive.

7. The amount of interstitial gland present depends upon the age of the rabbit.

8. Mature rabbits are more sensitive to gonadotropic substances than immature, a finding which agrees with that of other workers.

REFERENCES

(1) *Voge, Cecil I.:* Brit. M. J. **2:** 829, 1929. (2) *Kapeller-Adler, Regine:* Wien. klin. Wchnschr. **47:** 168, 1934. (3) *Bowman, D. E., Visscher, J. P., and Mull, J. W.:* Proc. Soc. Exper. Biol. & Med. **32:** 522, 1934. (4) *Bercovitz, Z.:* Am. J. Obst. & Gynec. **19:** 767, 1930. (5) *Collip, J. B.:* Canad. M. A. J. **22:** 215, 1930. (6) *Collip, J. B.:* Canad. M. A. J. **22:** 761, 1930. (7) *Fluhmann, C. E.:* Am. J. Obst. & Gynec. **22:** 803, 1931. (8) *Heim, K.:* Klin. Wchnschr. **10:** 357, 1931. (9) *Trancu-Ranier, Martha:* Zentralbl. f. Gynäk. **55:** 1971, 1931. (10) *Ofstad, B.:* Klin. Wchnschr. **11:** 1761, 1932. (11) *Heim, K.:* Klin. Wchnschr. **10:** 1031, 1931. (12) *Weisman, A., and Kleiner, I.:* Endocrinology **19:** 394, 1935. (13) *Snyder, F. F., and Wislocki, G. B.:* Bull. Johns Hopkins Hosp. **49:** 106, 1931. (14) *Soule, S. D., and Brown, T. K.:* Am. J. Obst. & Gynec. **23:** 44, 1932, (15) *Edwards, Dorothy:* Am. J. Obst. & Gynec. **23:** 694, 1932. (16) *Aronowitsch, G. D.:* Endokrinologie **7:** 113, 1930. (17) *Zondek, B.:* Zentralbl. f. Gynäk. **53:** 834, 1929. (18) *Evans, H. M.:* Proc. Soc. Exper. Biol. & Med. **26:** 595, 1929. (19) *Davy, Leita:* Endocrinology **18:** 1, 1934. (20) *Zondek, B.:* Arch. f. Gynäk. **144:** 133, 1930. (21) *Dickens, F.:* Biochem. J. **24:** 1503, 1930. (22) *Wiesner, B. P., and Marshall, P. G.:* Quart. J. Exper. Physiol. **21:** 147, 1932. (23) *Zondek, B., Scheibler, H., and Krabbe, W.:* Biochem. Ztschr. **258:** 102, 1933. (24) *Collip, J. B.:* Canad. M. A. J. **24:** 201, 1931. (25) *Fischer, F. G., and Ertel, L.:* Ztschr. Physiol. Chem. **202:** 83, 1931. (26) *Biedl, A.:* Endokrinologie **2:** 241, 1928. (27) *Katzman, P. A., and Doisy, E. A.:* J. Biol. Chem. **98:** 739, 1932. (28) *Katzman, P. A., and Doisy, E. A.:* Proc. Soc. Exper. Biol. & Med. **31:** 188, 1933. (29) *Idem:* Proc. Soc. Exper. Biol. & Med. **30:** 1188, 1933. (30) *Reiss, M., and Haurowitz, F.:* Ztschr. ges. Exper. Med. **68:** 371, 1929. (31) *Evans, H., Gustus, E., and Simpson, E.:* J. Exper. Med. **58:** 569, 1933. (32) *Reinhart, H. L., and Scott, E. S.:* J. A. M. A. **96:** 1565, 1931. (33) *Elden, C.:* J. Biol. Chem. **101:** 1, 1933. (34) *Janssen, S., and Loeser, A.:* Klin. Wchnschr. **10:** 649, 1931. (35) *King, A. G.:* J. Lab. & Clin. Med. **19:** 1033, 1934. (36) *Wilson, K. M., and Corner, G. W.:* Am. J. Obst. & Gynec. **22:** 513, 1931. (37) *Hirsch-Hoffmann:* Arch. f. Gynäk. **153:** 394, 1933. (38) *Sar-Louis, A. G.:* Endocrinology **19:** 314, 1935. (39) *Friedman, M. H.:* Am. J. Physiol. **90:** 617, 1929.

Winckler, H.: Narcosis a la reine and Preeclampsia, Monatschr. f. Geburtsh. u. Gynäk. **100:** 214, 1935.

Little attention has been paid to disturbances in the cardiovascular system as a cause of death in the toxemias of pregnancy. However, the electrocardiographic studies of Young have demonstrated that myocardial damage can be detected if systematic examinations are made many months after patients have had eclampsia. Winckler has observed acute cardiac failure in seven cases of preeclampsia during the past year and a half. In view of the fact that chloroform and chloral can produce harm to the cardiovascular system, Winckler is surprised that little mention is made of cardiac deaths during the course of the Stroganoff treatment of eclampsia.

For cases of preeclampsia he suggests a salt-free and protein-free diet. For the treatment of eclampsia he recommends immediate delivery. If operative interference in the form of a forceps delivery or a cesarean section is performed he employs a combination of chlorethyl-ether anesthesia. If convulsions occur after delivery, the author suggests that pernocton should be given in place of the chloroform-chloral hydrate routine recommended by Stroganoff. This will avoid damage to the heart.

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THE USE OF PITUITRIN INTRAVENOUSLY IN THE THIRD STAGE OF LABOR

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SINCE the introduction of pituitrin in obstetrics by Blair-Bell in 1909, no other drug has been exploited so extensively in this field of medicine. Each wave of enthusiasm has been followed by a similar period of adverse criticism, when many of the salient facts regarding its use were disregarded. During the past few years the intravenous use of pituitrin has again become prevalent; it may be well at this time to review its development.

In 1910 Foges and Hofstätter used pituitrin intravenously in two cases and observed that its action was quicker and more pronounced than when injected intramuscularly. It remained, however, for Hofbauer to discover the value of the drug in the treatment of postpartum hemorrhage, although in his original work he used it in the first and second stages of labor. He observed that the tetanic contractions usually occurred within a few seconds, but assumed a more normal course after several minutes had elapsed. In one of his papers, published in 1912, Hofbauer described the symptoms of what we now call pituitrin reaction. He often observed "pallor or slight cyanosis of the face, sweating, feeling of uneasiness or apprehension and apathy of the patient in labor." He furthermore reported satisfactory results in cesarean sections.

Continuing the work of Hofbauer, Sachs in 1914 and later in 1917, observed excellent results with this form of therapy during the third stage of labor, particularly in 12 cases of atony of the uterus. He was the first to suggest that hypertension might be a contraindication of its use, and in view of the criticism that marked relaxation followed the strong contractions, Sachs recommended that ergot be given before the action of pituitrin wore off. In spite of the fact that pituitrin was used intravenously both before and after the expression of the placenta, he noticed no ill effects. In fact, in 1917, he concluded that there was no other method which gave so prompt and sure an action as intravenous pituitrin.

The continued use of intravenous pituitrin met considerable opposition on the basis of animal experimentations and the strong influence of Stoeckel who, in 1925, objected to its routine use because of the supposed relaxation following its specific action. However, in 1926 Zorn recommended the use of this drug not only in the diagnosis of late ectopic pregnancy but also in outlining myomatous nodules in the pregnant uterus. Moreover, he employed it as an aid in teaching palpation to students, and suggested its use in ruptured uteri to control the bleeding from the smaller vessels. He never observed a case of incarcerated placenta.

In this country the use of pituitrin has been restricted to the third stage, mostly through the influence of the late J. Whitridge Williams. At the suggestion of Hofbauer, pituitrin has been used intravenously with good results since 1926 in Dr. Williams' clinic at the Johns Hopkins Hospital. Its use, however, has been limited to the period following the expression of the placenta.

Alden reported its use in the Boston Lying-In Hospital in 1933. He observed that the incidence of pituitrin reaction was greater when the patient had received pituitrin intramuscularly prior to the injection intravenously. Both he and Jackson, who discussed his paper, were convinced that its use had greatly decreased the incidence of packing. Alden felt that the pituitrin should be diluted with normal saline so that it can be given slowly.

Bohler and Reiles, agreeing with Stoeckel that tamponade of the uterus increased the mortality at least 100 per cent, reported a series of 200 cases in which they carried out manual exploration of the uterus, following the expression of the placenta, combined with 1 c.c. of pituitrin given intravenously. Their morbidity was slightly over 10 per cent with no mortalities.

The most recent and careful investigation was carried out by two Italians, Debiasi and Romussi, and reported in January, 1935. Using the Frey hysteogram, they found that the marked tetanic contractions occurred immediately after the injection and lasted from two to seven minutes. During the next seven to fifteen minutes, slight variations in contraction and relaxation were noted, but following this period the contractions became regular as in the normal cases. In their series of 54 cases they had 6 failures and 3 poor results, but they were able to explain these satisfactorily on the basis of other findings. They felt that intravenous pituitrin had no value in cases of placenta previa, since the bleeding was from the lower uterine segment which is not contractile. Because of the feeling of Poiche, Claude, Porak and Roulieu that pituitrin disturbs the conductive system of the heart and may cause complete dissociation, these investigators followed four of their cases with electrocardiograms, but could not substantiate such an observation, although they recommended that only 0.5 c.c. be used in cases with myocardial disease. Only one possible mild reaction was noted in all these cases.

More recently Baron has given 1 minim of pituitrin intravenously for induction of labor. He apparently obtained good results, although marked tetanic contractions with the loss of the fetal heart for periods as long as six minutes were often observed.

The present study consists of 96 cases of postpartum hemorrhage in which intravenous pituitrin was employed. It covers the period from September, 1934, to October, 1935, and does not include cases of cesarean section, although pituitrin intravenously is used routinely in these cases. The blood loss was measured by the method recently described by the author. For years we have arbitrarily taken 600 c.c. as the dividing line between normal and abnormal bleeding. However, because it has been shown by the author and other observers that the blood loss increases with the weight of the patient, and that conversely, the seriousness of the hemorrhage decreases with the weight of the patient, it would be better, from a prognostic and comparative standpoint, to express the blood loss in terms of the body weight. At the present time a detailed study is being conducted along these lines and the results will be presented in the near future.

Since the opening of the Woman's Clinic in September, 1932, pituitrin has been used intravenously in varying dosage. During this period, the dosage has been gradually reduced from 0.5 c.c. to 1.5 minims of surgical pituitrin (Units 20) diluted in 2.5 c.c. of normal saline. We feel that the smaller doses have the same therapeutic effect with a somewhat lower incidence of pituitrin reaction and that

the dilution makes it possible to give the medication slowly. For convenience and readiness we have found it advisable to have this dilution ready in the delivery rooms at all times. It is prepared daily by adding 1 c.c. of pituitrin to 24 c.c. of normal saline in a sterile flask sealed with a vaccine stopper. The required amount can be withdrawn quickly and with safety. We have not noted any deteriorating effect or increase in the incidence of pituitrin reaction.

In Table I the 96 cases are analyzed as to the cause of bleeding and the results obtained. Obviously the best results were obtained in the

TABLE I

DIAGNOSIS	CASES	GOOD CONTRACTION	CONTROL OF BLEEDING	REACTION
Atony	22	22	20	1
Partial separation of the placenta	14	14	14	1
Perineal and vaginal lacerations	12	12	5	0
Prolapse of uterus	14	13	2	1
Mismanagement, hemorrhage with placenta	13	11	4	0
Cervical lacerations	5	5	0	1
Myomata uteri	4	3	2	1
Placenta previa, marginal low implantation	4	4	3	0
Premature separation of the placenta	3	3	3	0
Retained placental tissue or membranes	3	3	0	0
Partial inversion of the uterus	2	1	1	0
Total	96	91	54	5

cases of true atony. There were two failures in this group, in one of which there was a question of prolapse of the fundus, since the bleeding stopped during packing when the uterus was brought up into the abdomen; and in the other, the patient had had a former cesarean section and the bleeding was possibly from the site of the previous uterine incision, since the fundus was well contracted. In the group in which the bleeding was due to partial separation of the placenta, the results were excellent but not necessarily due to the action of pituitrin. In these cases the bleeding occurred before the expression of the placenta, and following its removal, either manually, as was done in six cases, or spontaneously, the bleeding stopped, and the pituitrin was given more or less routinely because of the extent of the hemorrhage. The same is true in the cases of mild premature separation, although there was no evidence of excessive bleeding or atony. Only one case of marginal placenta previa is included, since the more severe types are usually treated by cesarean section. The other three cases are of low implantation of the placenta, according to the clinical history and the findings in the placentas. In all of these cases pituitrin intravenously had good results.

In the other cases, the intravenous pituitrin was helpful only so far as it controlled the bleeding due to atony associated with the main cause of bleeding. There was only 50 per cent success in the cases of myomata uteri. In one of these, packing was resorted to, and in another there was a secondary hemorrhage which required transfusions but no packing. The location of the myomas is probably responsible for this variation. One of the cases of partial inversion was a private patient and the condition was noticed several minutes after the patient had received pituitrin intravenously. This was corrected by packing. The other case of partial inversion occurred ten minutes after the expression of the placenta while clots were being expressed. This patient received pituitrin intravenously at that time and the inversion corrected itself without packing.

Notwithstanding the investigation of Debiasi and Romussi, one should realize the possibility of relaxation after the strong tetanic contraction, and ergot or other oxytocics should be given. In one of our cases pituitrin alone was used intravenously, and five hours after delivery there was a secondary hemorrhage of 500 c.c. and evidence of mild shock. Such bleeding could have been prevented by the administration of other stimulants in addition to the pituitrin intravenously.

In five of our cases there was a pituitrin reaction, as manifested by cyanosis, disturbance of the pulse rate, and appearance of shock. In one case a bradycardia of 40 was noted, while in the others a tachycardia was the prominent feature. While most of these reactions were mild and temporary, serious consequences may result, as was shown in one of the cases. This patient died a short time after delivery, and since the cause of death has not been definitely determined, it is conceivable that it was due to pituitrin given intravenously. A résumé of the clinical history is as follows:

The patient was thirty-nine years of age and had had two miscarriages but no full-term pregnancies. She presented herself to the gynecologic clinic with the history of amenorrhea of four months' duration. The diagnosis of pregnancy complicated by myomata uteri was made, and because of a systolic murmur over the apex, she was subsequently examined by the cardiac consultant who ruled out the possibility of cardiac disease. She was followed in the dystocia clinic for several months and during that time the myomatous nodule, which was about 9 cm. in diameter and completely filling the culdesac during the early months of pregnancy, had risen into the abdomen. The pelvis was measured as normal. The patient was admitted to the hospital in mild labor on Jan. 28, 1935. At that time there was no evidence of disproportion, the fetal head being just above the spines. After a labor of twenty-six hours, with a second stage of fifteen minutes, the patient was delivered by midforceps because of fetal distress, the fetal heartbeat being 80 per minute. Up to this time the patient's condition had remained good, the pulse and respirations being normal. There was no evidence of cardiac failure. The placenta was expressed five minutes later without difficulty. Following this, there was some bleeding from the episiotomy but none from the uterus. Because of the diagnosis of myomata uteri, 1.5 minims of pituitrin were given intravenously. Two minutes later, the blood loss being 400 c.c., the patient began to show evidence

of shock. The pulse was of poor quality and ranged around 160. There was cyanosis of the face and the blood pressure could not be obtained. Intravenous glucose (10 per cent) was given and her condition improved, the systolic pressure being 90. Believing that this reaction was due to shock, and since there was still slight bleeding from the episiotomy, 1 c.c. of pituitrin was given intramuscularly thirty-three minutes after the intravenous injection. Five minutes later the patient's condition suddenly became worse. The respirations became shallow, the blood pressure could not be obtained, and frothy bloody sputum appeared at the mouth. In spite of caffeine, adrenalin, and atropine the respirations ceased ten minutes later. The impression at the time was cardiac failure with pulmonary edema. The total blood loss was measured as 700 c.c. An autopsy was not obtained.

The significant facts in this case are: (1) The intravenous pituitrin was given prophylactically, since there was no atony or uterine bleeding, and (2) evidence of shock appeared after each of the injections. Although this is not a clear-cut case of death due to pituitrin reaction, it should impress upon us the fact that any medication which produces a generalized reaction, however mild and temporary it may be, might in some cases produce serious and lasting effects.

The cause of these reactions is not yet clear. In this series, most of the patients had received pituitrin intramuscularly prior to the intravenous injection, and this may account for the high incidence of reactions. Moreover, in our own experience, pituitrin reactions are seldom noticed in cases of cesarean sections where general anesthesia is used. These observations support the theory of Alden that pituitrin reactions are manifestations of sensitivity to the drug. For that reason we are employing, at the present time, an equivalent amount of pitocin which is protein-free.

Table I shows that pituitrin was given intravenously in practically all types of bleeding. It was of no therapeutic value in 42 of the 96 cases. This is due to the prevailing impression that most of the postpartum hemorrhages are due to atony of the uterus. In fact only 23 per cent of the hemorrhages in this series, and 9 per cent in a series previously studied, were due to this cause. Every physician should be familiar with all the causes of bleeding in each of the three phases of the third stage. Partial separation of the placenta, cervical lacerations, and episiotomies or perineal lacerations are the most frequent causes of bleeding before the expression of the placenta. Excessive bleeding with the expression of the placenta is due to faulty management of the third stage of labor. Following the expression, atony, prolapse of the fundus, and cervical and perineal lacerations are the most frequent factors in the production of excessive blood loss. With such knowledge, the suitable therapy can be instituted immediately. If atony is present, and this can be determined quickly, it is useless to attempt to control the bleeding with intramuscular injections of pituitrin or ergot since they require four to five minutes to act. Intravenous therapy should be instituted at once. Of course, permanent

advancement along this line will be made only when we discover the causes of atony and thereby eliminate them. More extensive researches in the field of analgesia and anesthesia are necessary.

Another factor which is increasing the blood loss is the tendency to wait ten or fifteen minutes before attempting to express the placenta. Such a practice must be condemned, for the placenta should be expressed as soon as it is separated, regardless of the time elapsing between the delivery and the expression. Such a delay will only lead to the formation of clots behind the placenta and subsequent atony of the uterus. We must appreciate this point, as was so well stated by one of our internes in explaining a hemorrhage due to this cause: "At the time it did not seem rational that the placenta had separated immediately following the delivery of the child."

CONCLUSIONS

1. From the literature and our own experience, intravenous pituitrin in the third stage of labor is reliable, quick, and intense in its action. It is specific for atony of the uterus only.

2. One and a half minims of surgical pituitrin (Units 20), diluted in 2.5 c.c. of normal saline, are used in this clinic. This dilution makes it possible to give the medication slowly.

3. Reactions were noted in 5 of the 96 cases. In one of them it may have been responsible for the death of the patient.

4. Intravenous pituitrin should not be used indiscriminately, but only in the cases of atony of the uterus. In these cases it should be given as soon as the diagnosis is made. Intramuscular injections of pituitrin or other oxytocics are useless in the control of atony because they require four to five minutes to produce the desired effect.

5. Atony of the uterus is not the only cause of postpartum hemorrhage. It was responsible for only 23 per cent of the hemorrhages in this series. A knowledge of the management of the third stage and of the other causes of excessive blood loss is indispensable.

REFERENCES

(1) *Alden, C. R.:* New England J. M. **209:** 1211, 1933. (2) *Baron, H. A.:* J. Obst. & Gynec., Brit. Emp. **42:** 322, 1935. (3) *Bohler, E., and Reiles, M.:* Gynecologie et Obstetrique **29:** 393, 1934. (4) *Debiasi, E., and Romussi, P.:* Clin. Ostet. **13:** 2, 1935. (5) *Foges, A., and Hofstätter, R.:* Zentralbl. f. Gynäk. **34:** 1500, 1910. (6) *Hofbauer, J.:* Med. Wchnschr. **1:** 1210, 1912. (7) *Pastore, J. B.:* Am. J. Obst. & Gynec. **29:** 866, 1935. (8) *Idem:* Am. J. Obst. & Gynec. **31:** 78, 1936. (9) *Sachs, E.:* Monatschr. f. Geburtsh. u. Gynäk. **40:** 544, 1914. (10) *Sachs, E.:* Monatschr. f. Geburtsh. u. Gynäk. **45:** 399, 1917. (11) *Zorn, W.:* Zentralbl. f. Gynäk. **1:** 1315, 1926.

FETAL HEART DILATATION; PULMONARY CONGESTION AND PULMONARY EDEMA NEONATORUM; "CONGENITAL PNEUMONIA"; ASPHYXIA*

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UP TO quite recently, asphyxia was considered the main cause of death of the fetus in utero and of the stillborn. The seat of the trouble was believed to be primarily in the respiratory system. All efforts were therefore concentrated on getting air into the child's lungs, and drastic methods were used which were frequently injurious. Very little consideration was given to the underlying causes that interfered with the proper functioning of the respiratory apparatus.

With the performance of more frequent autopsies, it has become evident that asphyxia is not the primary or underlying cause of death of the fetus in most cases, but that asphyxia is secondary to other conditions. Injuries to the fetus, in which cerebral hemorrhage is the main lesion, were found to be the most frequent cause of asphyxia and the death of the fetus. But there still remain a great number of unexplained or wrongly interpreted cases of fetal and neonatal deaths.

When the fetus dies before birth from compression of the cord, the separation of the placenta or from any other cause, it is believed that, due to the increase of CO_2, the fetus first makes an effort to breathe, and as respiration is impossible, it is asphyxiated. But that is not necessarily the way death occurs, for the accompanying decrease in oxygen, anoxemia, depresses the vital centers, and the fetus dies, in most cases, without the respiratory center being stimulated to action and without the fetus making any attempts at respiration. These deaths, therefore, cannot be designated as due to asphyxia.

Atelectasis as a cause of neonatal death is, I believe, grossly exaggerated. Infants, the same as adults, can live with a considerable portion of their lungs collapsed. Atelectasis as a primary condition occurs rather infrequently.

Johnson and Meyer state: "It should be recognized that in all cases atelectasis is secondary to some primary cause." The real cause of death is the primary condition. When on autopsy a baby shows atelectasis, we should determine further what lesion prevented the lungs from expanding. The term atelectasis as a cause of death is used mostly to cover up unknown causes.

The respiratory apparatus does not function during intrauterine life. It is fully developed at about seven months, but lies dormant until the time comes for it to be set in motion by the proper stimulus. When the baby is born, the placenta separates immediately, and the consequent

*Read at a meeting of the Section of Obstetrics and Gynecology of the New York Academy of Medicine, December 17, 1935.

increase of CO_2 in the placental-fetal circulation together with the external skin irritation stimulate the respiratory apparatus so that the baby breathes. When respiration is delayed or when the infant fails to breathe, the assumption is that the respiratory apparatus is at fault and the condition is designated as asphyxia. But as the respiratory apparatus does not function intrauterine, it is not subjected to any strain and is, therefore, not likely to be out of order. When it fails to react, it is due to a lesion in some vital structure or to a failure of the proper stimulus to reach the respiratory center. As the stimulus to the respiratory center comes through the circulation, it is to the circulatory system that we must give our attention and determine the factors that disturb it.

In a previous paper entitled, "The Slowing of the Fetal Heart and Its Relation to the Fetal-Placental Circulation," I indicated that the slowing of the fetal heart is not due to an increase of CO_2, which is supposed to stimulate the vagus, but that it is produced directly by the contraction of the uterus, compressing the placenta and forcing a variable amount of blood out of the placenta into the fetus. This increases the volume of blood in the fetus and raises the arterial and venous tension in the fetal circulation. This increased tension produces the slowing of the fetal heart (Figs. 1 and 2). The increased volume of blood and increased tension produce a syndrome, of which the slowing of the fetal heart is one of the early manifestations. The syndrome includes, in addition to the slowing of the fetal heart, the passing of meconium, the stopping of the heart, hemorrhages in the fetal organs, death of the fetus at the onset of labor, and other manifestations.

The increased tension in the fetal-placental circulation also produces congestion and hemorrhage in the placenta itself. This accounts for the lesions recently described by Goodall, which he found in two-thirds of the placentas examined.

The overloading of the circulation also directly overloads the fetal heart. The auricles and ventricles are overfilled with blood, the heart becomes distended and dilated, it is prevented from contracting, and therefore ceases to function. Consequently a condition of acute cardiac dilatation occurs in the fetus.

When the overloading of the circulation occurs with the last one or two labor pains, and the baby is delivered, the baby's heart will still be overloaded and dilated. When the infant starts breathing and the lungs expand, there is a stasis in the pulmonary circulation due to the dilated heart, and as a result of it, pulmonary congestion occurs. This is made evident by crepitant râles which can be heard over the chest. The râles will vary in extent depending upon the degree of congestion.

When the overloading of the heart is more severe, particularly in those cases where the fetal heart rate had dropped so low that it had been necessary to deliver the baby quickly, the dilatation of the heart is

greater, the pulmonary stasis is more severe, so that besides the congestion there occurs a pulmonary edema. This is evidenced by bubbling râles over the entire chest, with considerable quantities of serum in the mouth and throat.

These physical signs were ascertained by listening to the chest with a (sterile) stethoscope as soon as the babies were born. When the baby is delivered it is held up by its legs for a few seconds, until it takes

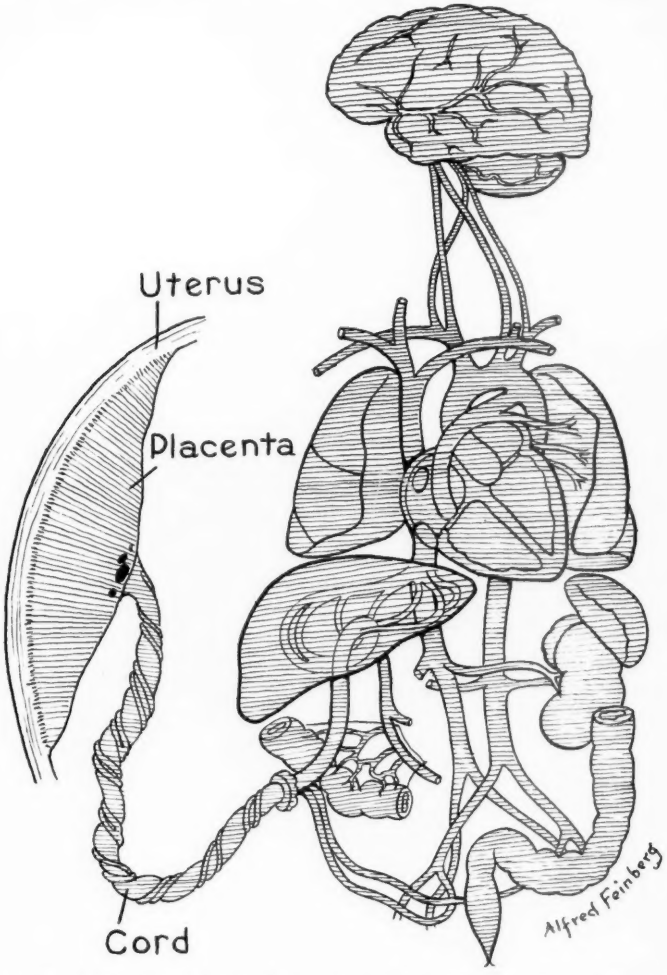

Fig. 1.—The fetal-placental circulation in the interval between a labor pain. The light shading represents the circulation in the blood vessels and organs under normal tension.

one or two good breaths, and to permit the contents of the mouth and throat to drain out. It is then laid down and the chest is auscultated. In the great majority of cases the normal breath sounds with the normal heart sounds can be heard, but where there has occurred some embarrassment of the circulation, as evidenced by the slowing of the

fetal heart, we get the signs of pulmonary congestion, and less frequently the signs of pulmonary edema.

As the heart regains its tone, the congestion and edema clear up and the sounds become normal. I have not as yet used any medication for this condition. It might be advisable to treat the condition as we usually do cases of cardiac dilatation with pulmonary edema.

With the pulmonary congestion and pulmonary edema, there may also take place, due to the increased tension in the circulation, rupture of the

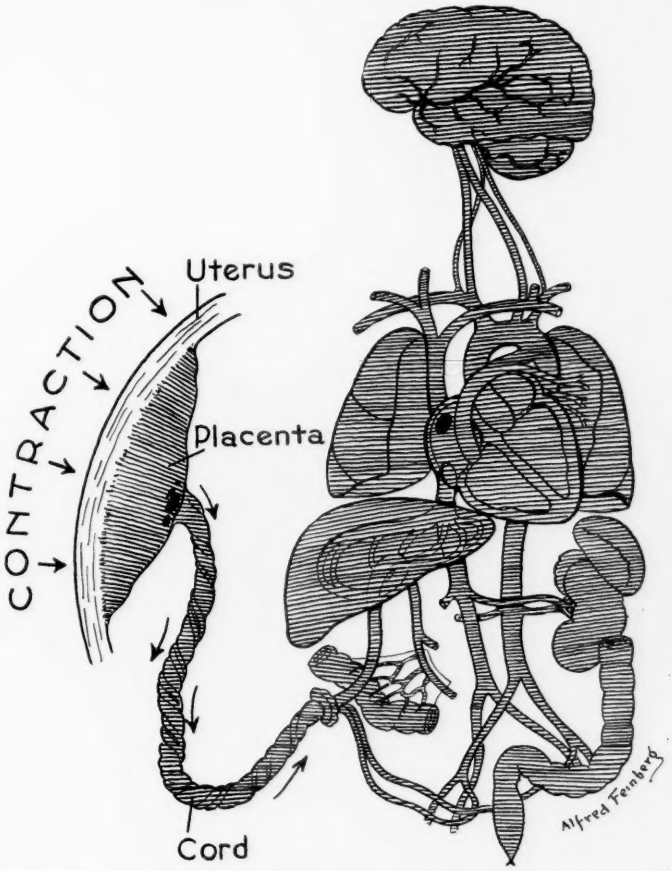

Fig. 2.—The fetal-placental circulation during a strong uterine contraction. The placenta is compressed and blood is forced out of the placenta into the fetus. The dark shading represents the increased tension in the circulation, with the blood vessels distended, the heart dilated, and the organs congested.

blood vessels in the lungs with the bringing up of fresh blood. The condition then becomes much more serious.

We should give some consideration to the possible damage that the heart may sustain from such intrauterine cardiac dilatation. If the baby survives we must consider whether the heart recuperates entirely or whether it remains permanently weakened. It is possible that the

shortness of breath of some children and their inability to exert themselves, which may be associated with poor heart tones, are the result of this cardiac strain at the very beginning of life. This condition of the heart warrants further study.

As the baby is held up by its legs with the head down, all the contents of the bronchi, trachea, throat, and mouth should run out. But frequently serum and mucus accumulate in the throat again. It has been rather puzzling how to account for the source of this mucus. It has always been assumed when the infant's chest is "full of mucus" that it had swallowed or rather aspirated the mucus in its passage through the birth canal. But that is not so, as in head presentations we know that the baby does not breathe until the head has left the vagina. It had to be presumed that it swallowed this mucus when no other explanation was forthcoming. It is my belief that the "mucus" in the chest is not aspirated, but that it is the amniotic fluid normally present in the respiratory tract, and the serum of pulmonary congestion or pulmonary edema caused by the dilatation of the fetal heart. When the infant's mouth and throat continue to fill up with serum, crepitant or bubbling râles can be heard in the chest; and conversely as long as these râles are present the infant continues bringing up serum from the lungs.

In considering the trachea and bronchi in the fetus, one gets the impression from textbooks and the literature that in the fetus they are empty and do not contain anything. A consideration of the anatomy of these structures will show that this is not possible. The trachea and bronchi have cartilaginous rings in their walls which hold them open and prevent them from collapsing. Any cavity whose walls cannot be approximated must hold something, it cannot remain a vacuum. In the world at large all so-called empty spaces are filled with air, but as there is no air intrauterine when the membranes are intact, the trachea, bronchi, and bronchioles must be filled with whatever substance that surrounds them. Therefore, these cavities in the fetus must be filled with amniotic fluid. As respiration does not take place intrauterine, there is nothing unphysiologic or objectionable in having amniotic fluid occupying these spaces. The amniotic fluid fills all the open cavities in the fetus, such as the external ear, the nose, mouth, throat, trachea, and bronchi. The amniotic fluid does not normally enter the lungs, as the lungs are collapsed, although it is possible that amniotic fluid does penetrate some of the proximal alveoli.

When the membranes rupture and the amniotic fluid escapes, air enters the uterine cavity. The amniotic fluid then can run out of the bronchi, the trachea, and mouth, and can be replaced by air. This occurs in head presentations, but in breech presentations, as the head is at a higher level than the trachea, the amniotic fluid cannot drain out, not until at the time of delivery, when the body is raised above the level of the head.

A number of observers have described a condition which they have found at autopsy in the lungs of stillborn infants, and in those that have died soon after birth, as congenital pneumonia. Some of the later papers on the subject are by Johnson and Meyer, Farber and Smith, Kalder, and Warwick.

It is believed that this form of pneumonia starts during intrauterine life and is produced either by bacteria or amniotic fluid or both. But all the observers of this condition find difficulty in explaining how bacteria could get into the fetus to cause the pneumonia. Also, to account for the fact that bacteria were found in only a small percentage of the cases, and only in those babies that lived for some time or in which the autopsy was not done promptly. The theory that amniotic fluid by chemical irritation may be the cause of these pneumonias is assumed because the bacterial cause fails to satisfactorily account for the condition. Clinically, the infants do not have any fever and do not show physical signs or symptoms of pneumonia. Pathologically, on gross examination the lungs do not suggest pneumonia, there is no pleuritis, the lesions are always bilateral, and resemble hemorrhage, and atelectasis with congestion. The diagnosis of pneumonia is made entirely on the microscopic findings.

It is my belief that this pathologic condition is not pneumonia in most of the cases so considered. The condition is a pulmonary congestion, pulmonary edema, and pulmonary hemorrhage, produced by the overloading of the fetal circulation in the manner already explained above. This condition may be associated with fetal heart dilatation, or with hemorrhage in the brain or other organs. The amniotic fluid that is found at autopsy in these "congenital pneumonias" comes from the trachea and bronchi which, as indicated above, normally occupies these cavities. As the condition is not pneumonia, there is, therefore, no need of trying to explain its exciting cause by bacteria or by amniotic fluid irritation.

It occasionally happens that a baby delivered by cesarean section and not subjected to unsuccessful attempts at delivery or to a prolonged labor is, for no apparent reason, stillborn. The death of the baby may be due to the practice of some operators of ordering the intramuscular injection of an ergot preparation, while they are scrubbing up, or the injection of pituitrin at the start of the operation, in order to have the uterus contract sooner and lessen the bleeding. But apparently little consideration is given to the effect these injections can have on the fetus in the meantime. The ergot or pituitrin in some cases causes a tetanic contraction of the uterus, which compresses the placenta and forces blood out of the placenta into the fetus, thereby overloading the fetal circulation, and stopping the fetal heart or causing hemorrhages in the vital organs and death of the fetus.

The authors of the papers on "congenital pneumonia" mention cases which were delivered by cesarean section and were stillborn, and on autopsy they found lesions in the lungs which they assumed to be pneumonia. This was accompanied in some cases by hemorrhages in other organs. They are at a loss to explain how the pneumonia occurred. As indicated above, these lesions are not pneumonia but congestion and hemorrhage, and death was caused by the overloading of the fetal circulation.

Another cause of fetal death during cesarean section is due to the excess loss of blood from the fetus. In incising the uterus, the placenta is often cut through and blood escapes from the placenta and consequently from the fetus. While a variable amount of blood can escape from the placenta without any serious effect on the fetus, we cannot judge the amount that the fetus is losing or how much loss it can stand without serious consequences. A fatal exsanguination may occur in a very short time. If the incision in the placenta happens to be near the insertion of the cord, the bleeding will come directly from the fetus and the fetus will succumb sooner. It is, therefore, advisable, when the placenta is cut into, to search for the cord and clamp it immediately before delivering the baby.

As a rule, respiration is delayed longer in cesarean babies than in those delivered from below. The reason for this is, I believe, because of the loss of blood from the incised placenta, an anemia is produced in the fetus, which delays the stimulation of the respiratory center. Also after forceps delivery the baby does not breathe as promptly as it does in spontaneous deliveries. In a spontaneous delivery, the contraction of the uterus forces the baby out, and at the same time forces blood from the placenta into the fetus; the respiratory center, therefore, receives an abundant supply of blood and is promptly stimulated. In forceps delivery and in cesarean section, the uterus is not sufficiently contracted while the baby is being extracted, so that the placenta is not compressed and the baby thereby gets less blood in its system and this delays the stimulation of the respiratory center.

As the circulatory system plays such an important rôle in the welfare of the fetus, the necessity of constantly watching the fetal heart is evident. During the second stage of labor, it is not sufficient to listen to the fetal heart occasionally, but it is necessary to watch the fetal heart rate constantly. Toward the end of the second stage it is absolutely essential that the fetal heart be auscultated after each and every pain. Babies are frequently lost with the last one or two labor pains. When the head is on the perineum and the uterine contractions are strong, the fetal circulation is then under the greatest tension and the fetal heart may be dangerously embarrassed. Babies are thereby lost in the last few minutes of delivery. Holding the head back for any length of time to protect the perineum is not good practice, as it does not save the

perineum and endangers the child. An episiotomy done at this stage is of greater advantage to the perineum and a relief to the baby.

With the writer's heavy-weighted stethoscope the nurse can easily auscultate the fetal heart while the woman is on the delivery table, without disturbing the sterile drapes. When the fetal heartbeat remains normal until the end of the delivery, the baby is bound to be in good condition when it is delivered and will not need resuscitation. The most important part in the treatment of asphyxia neonatorum is its prevention; and that can be accomplished by watching the fetal heart constantly, and avoiding injury to the baby during delivery.

When the baby is born, it should be held up by its legs with its head down. This is the best means of having the amniotic fluid drain out of the baby's mouth, throat, trachea, and bronchi. This allows gravity to clear out all the passages. Suction with a catheter cannot clear out the trachea or bronchi as effectively as gravity. While the child is in the inverted position, the lower jaw is compressed against the upper jaw, and with outward pressure from the neck to the chin the contents of the mouth are expelled.

When the baby is held in the inverted position, more blood goes to the medulla and stimulates the respiratory center sooner. I find that babies breathe sooner if they are held in the inverted position than when they are laid down as soon as delivered.

As stated above, when the fetal heart rate has been good and the baby is not injured, the baby should breathe in a few seconds after it is born. When it fails to breathe, the child should receive immediate attention. All violent methods, rough handling, and cold plunges are condemned. But we cannot leave the baby alone entirely with the hope that it will start breathing. At birth the baby is in a state of apnea, with the accumulation of CO_2, the hypercapnia stimulates the respiratory center. But while CO_2 is accumulating and the baby does not breathe, there occurs at the same time a diminution of oxygen, producing a state of anoxemia. This anoxemia can in the meantime depress the medulla to such an extent that the CO_2 will fail to stimulate it to action. For that reason it is not advisable to wait any length of time before getting the baby to breathe. Delayed respiration or improper heart action causing a stasis in the circulation at birth may so interfere with the proper oxygenation of the vital centers and the brain as a whole, that they may become damaged in a very short time. Anoxemia is a dangerous condition, especially for the immature brain cells of the newborn. As Haldane says, "Anoxemia not only stops the machine but wrecks the machinery." It is possible that the child may suffer permanent damage as a result of the temporary anoxemia. The retarded mentality of some children, coming from intelligent parents, may be due, aside from other causes, to damage to the brain sustained at the time of birth from anoxemia.

In order to avoid delay in respiration, if the baby fails to breathe spontaneously and promptly, mouth to mouth respiration should be used. I prefer this method to any other, as it is immediately available and is most effective. The baby should be kept warm during the procedure. I consider the time element an important factor. With this method a heart that is hardly perceptible or very slow commences to beat forcibly and more rapidly. While if we wait for other means of resuscitation, the heart may stop entirely in the meantime.

SUMMARY

1. Asphyxia as a cause of fetal and neonatal death is usually secondary to some other lesion; as a primary cause it occurs rather infrequently.

2. Death of the fetus intrauterine is not produced through asphyxia but directly from anoxemia.

3. Atelectasis as a primary cause of death occurs rarely, it is mostly secondary to, and associated with, other lesions.

4. It is the circulatory system that is most frequently involved in the death of the fetus.

5. The contraction of the uterus compresses the placenta and forces blood out of the placenta into the fetus and overloads the fetal circulation. This produces a syndrome, which includes the slowing of the fetal heart, the passing of meconium, the stopping of the fetal heart, hemorrhages in the fetal organs, death of the fetus at the onset of labor; and fetal heart dilatation, which in turn causes pulmonary congestion and pulmonary edema neonatorum.

6. When the baby's chest is "full of mucus" it is due to pulmonary congestion and pulmonary edema, and only occasionally to aspiration.

7. The trachea and bronchi of the fetus are not empty, but are filled with amniotic fluid.

8. "Congenital pneumonia" cannot be considered as an entity, the pathologic findings are due to pulmonary congestion, pulmonary edema, and pulmonary hemorrhages.

9. In cesarean section, death of the fetus may be due to the overloading of the fetal circulation from the use of pituitrin or ergot. Also from the excess loss of blood from the incised placenta.

10. Delayed respiration at birth produces anoxemia which may cause damage to the brain.

REFERENCES

Adair, Fred L., and Schumann, E. A.: Obstetrics and Gynecology, edited by Curtis, A. H.: Philadelphia **1**: 1933, W. B. Saunders Co., p. 513. *DeLee, J. B.*: Obstetrics, Philadelphia, 1934, W. B. Saunders Co. *Farber, S., and Sweet, L. K.*: Am. J. Dis. Child. **42**: 1372, 1931. *Goodall, James R.*: Am. J. Obst. & Gynec. **30**: 577, 1935. *Haldane, John S., and Priestley, J. G.*: Respiration, New Haven, 1935, Yale University Press. *Johnson, W. C., and Meyer, J. R.*: Am. J. Obst. & Gynec. **9**: 151, 1925. *Kaldor, J.*: Am. J. Obst. & Gynec. **25**: 113, 1933. *Leff, M.*: Am. J. Obst. & Gynec. **24**: 898, 1932; **18**: 868, 1929; **20**: 108, 1930. *Rothman, P. E.*: West. J. Surg. Obst. & Gynec. Nov., 1934. *Warwick, M.*: Am. J. M. Sc., p. 253, 1934.

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AN OPERATION TO CORRECT GENITAL PROLAPSE FOLLOWING VAGINAL PANHYSTERECTOMY*

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THERE is still considerable difference of opinion as to which is the best operative procedure in the treatment of complete uterine prolapse. Some routinely employ the Mayo operation, which has as one of its important steps the vaginal removal of the entire uterus. One advantage of this operation is that the possibility that the patient may develop a uterine carcinoma in later life is entirely eliminated. On the other hand, another group of gynecologists prefer the Watkin's interposition operation, or vaginal fixation as it is sometimes called, for cases of prolapsus uteri and reserve the vaginal panhysterectomy for those patients who have in addition to the prolapse other pathologic conditions in the uterus, such as small fibroids.

An interposition operation is easier to perform and less shocking than a vaginal panhysterectomy, but the main reason for my own preference for the former operation is that it has yielded such excellent results. In 1926 I reported a series of 60 patients with uterine prolapse operated upon by Cullen and myself and studied postoperatively. One woman had a return of the cystocele after being well for ten years. In the other 59, all of whom were traced, the interposition operation apparently permanently cured the prolapse. Everett[2] reported a postoperative study of the cases operated upon at the Johns Hopkins Hospital for uterine procidentia and compared the results obtained by the interposition operation with those following vaginal panhysterectomy. He concluded that the Watkin's interposition operation is the procedure of choice for the treatment of prolapse of the uterus in women past the menopause.

The interposition operation certainly has this one most important advantage over a vaginal panhysterectomy, namely, that when failure occurs a much more serious condition develops when the uterus has been removed. When an interposition fails, there is usually merely a return of the cystocele or rectocele and a simple plastic operation will correct the condition; and even if the uterus comes down, one can still try the interposition operation again, suturing the fundus of the uterus to the periosteum of the symphysis as recommended by George Gray Ward.

On the other hand, when a genital prolapse develops after a panhysterectomy, a condition results which is more difficult to correct.

*Read before the Baltimore Obstetrical and Gynecological Society on February 15, 1936.

In fact some gynecologists feel that no satisfactory operative technic has yet been worked out for curing such a prolapse. The anterior and posterior vaginal walls roll out and become lengthened, and before long a true hernia of the pelvis develops. Probably a colpectomy has been the operation most frequently performed for genital prolapse after a panhysterectomy, but it is difficult to carry out properly and if successful the sexual life of the woman comes to an end.

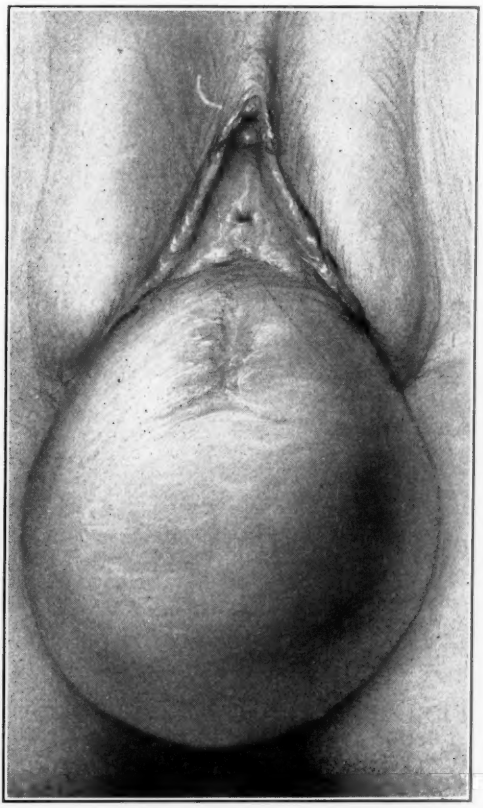

Fig. 1.—Shows the genital prolapse. The scar from the previous operation (a vaginal panhysterectomy) can be plainly seen.

One year ago I had the opportunity of operating upon a patient with a marked genital prolapse following vaginal panhysterectomy. The condition was entirely corrected by the operation. The woman now has no urinary symptoms and the bladder has a capacity of 500 c.c. Moreover she has been left with a vagina of normal length and diameter so that sexual relations are possible. The operation performed on this patient, while not demonstrating any entirely new principles, does bring out certain modifications in technic which, I believe, have not been previously reported.

A. M., aged fifty-eight, was admitted to St. Joseph's Hospital, Baltimore, May 3, 1935, complaining of vaginal prolapse. The family and general history were unimportant. The menstrual periods stopped at the age of fifty. The patient had had three children. She had noticed for ten years that "her womb came down." She had been operated upon in December, 1933, for uterine prolapse at one of the Baltimore hospitals. While in the hospital, she was found to have diabetes mellitus for which insulin was prescribed. Within a few months after the operation the patient again noticed that "something came down." She tried using a ring pessary but this gave no relief. She decided to submit to another operation and was admitted to my service at St. Joseph's Hospital. The general physical examination was essentially normal. The urine showed a small amount of sugar which promptly disappeared when the patient's daily dose of insulin was slightly increased. Pelvic examination showed that there was a marked genital prolapse. When the patient strained or stood up, the apex of the prolapse descended 10 cm. below the vaginal orifice. There was fortunately no ulceration of the prolapsed tissues. The patient was kept in bed several days prior to operation, and daily vaginal douches were given.

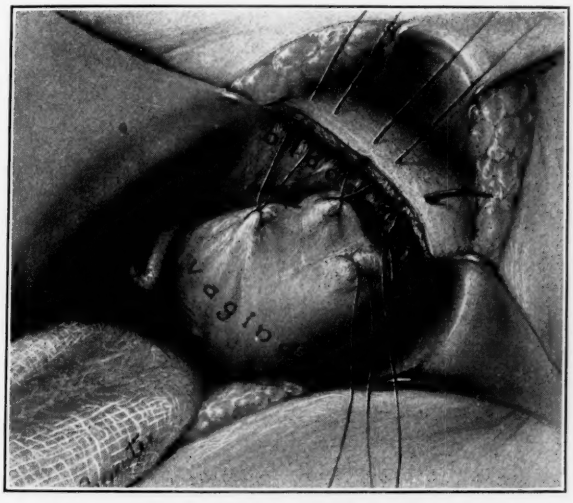

Fig. 2.—The vagina is being sutured to the lower part of the abdominal fascia. This pushes the bladder forward. The recti muscles are shoved laterally as the stitches are introduced through the peritoneum and fascia. It is to be noted that the fascia in the lower part of the wound has not been divided, although the skin incision goes all the way down to the symphysis pubis. One of the elongated round ligaments can be seen on the left side of the picture.

Operation: May 14, 1935. The vagina was first carefully scrubbed with soap, alcohol, and ether, and then painted with Scott's solution. A midline incision through the skin and fat was then made from a little below the umbilicus down to the symphysis pubis. The fascia and peritoneum were divided in the upper half of this incision but not in the lower half. An assistant with his finger in the vagina then pushed the prolapse upward until the vagina could be clearly identified by the operator. A Cameron light introduced from below into the upper part of the vagina facilitated the identification of structures. The bladder itself had hypertrophied as a result of being prolapsed for so many years. Three medium-sized braided silk sutures were then introduced from above into the top of the vaginal vault which had been pushed upward by an assistant. These sutures were made to pass through the peritoneum, to pass on either side medially to the recti muscles which were pushed laterally, and finally to pass through and come out above the fascia of the recti muscles. The two ends of each of these sutures were then tied together above

the fascia of the recti muscles. This step in the operation fixed the vagina to the anterior abdominal wall with three mattress sutures. One of these sutures passed directly through the midline and the other two were close to it. All were medial to the inner borders of the recti muscles. When the operation was completed, the knots lay above the fascia but below the skin and subcutaneous tissue. Two points in technic should be emphasized. First, that these sutures do not go through the skin and, second, that they must be of nonabsorbable material. They are per-

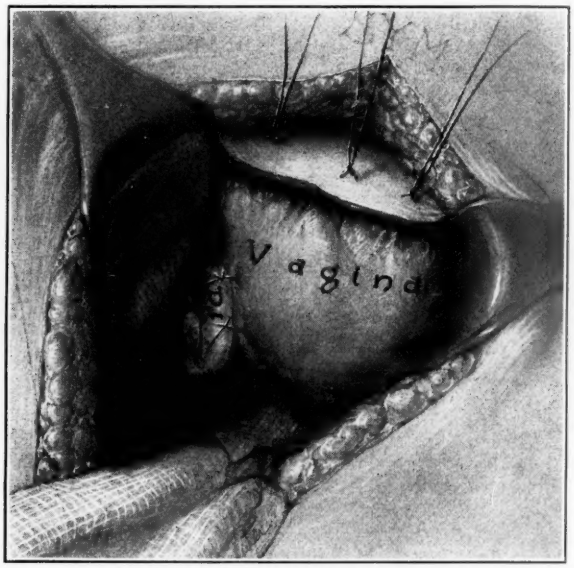

Fig. 3.—The vagina has now been sewed to the peritoneum and rectus fascia. In order to prevent the bladder from bulging laterally around the vagina which does not reach all the way across the pelvis, the elongated round ligaments are plicated and sutured to the vagina. The drawing shows this step in the operation completed on the left side.

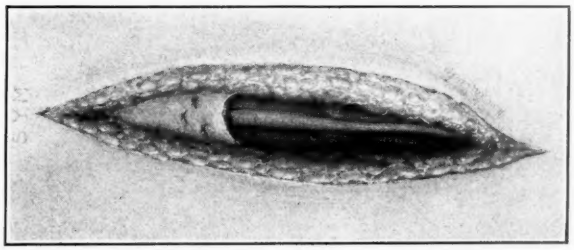

Fig. 4.—Shows the position of the fixation sutures after they have been tied and indicates the approximate length of the skin and fascial incisions. One of the fixation sutures lies directly in the midline and the other two are close to the midline. They have all been brought through the peritoneum and fascia medial to the rectus muscles.

manent sutures and not to be removed after a few weeks. In these and several other features this operation differs from the one described by Fraenkel, in 1920, and recommended by Jarcho in an article published in 1928.

In the former operation upon this patient the surgeon had followed the usual procedure of sewing the round ligaments back to the vaginal vault after he had removed the uterus. As the genital prolapse developed after the hysterectomy, the

round ligaments were stretched and became lengthened. Now in the second operation, as the vaginal vault was drawn up, the round ligaments were also drawn upward. On either side of the vagina, which was now fixed to the anterior abdominal wall, the round ligaments appeared V-shaped. One leg of the V started at the place at which the round ligament entered the peritoneal cavity from the inguinal canal, and then dipped down into the pelvis for some distance. The round ligament finally turned upward again ending as the top of the other leg of the V at the point where the vagina was now attached to the abdominal wall. Of course, I do not know whether or not the round ligaments would always lengthen in cases of genital prolapse in the way that they did in this case, but certainly this V-shaped formation exhibited by both round ligaments was of definite help in operating upon this patient. For while it was evident that the fixation of the vagina to the anterior abdominal wall would correct the vaginal prolapse, it appeared as if the hypertrophied bladder which now could not prolapse in the midline because of the diaphragm which the vagina now formed in the midline, could still bulge laterally around this diaphragm, but by employing the additional procedure of sewing the two limbs of the V-shaped round ligaments together on either side and to the vagina, these lateral openings were closed, thus helping to hold the bladder forward and preventing it from getting around the vagina. After completing the abdominal operation a perineorrhaphy was performed. There was no necessity for performing an anterior repair, as the abdominal operation had already entirely corrected the cystocele.

The convalescence was uneventful, and she was discharged from the hospital on the twenty-second day after operation. On examination nine months later there was no evidence of any prolapse, either anteriorly or posteriorly, and two fingers could be introduced into the vagina for 10 cm. without causing the patient any discomfort. The bladder has a capacity of 500 c.c. The patient has no urinary symptoms and no other complaints.

REFERENCES

(1) *Brady, L.:* Surg. Gynec. Obst. **43:** 476, 1926. (2) *Everett, S. H.:* Surg. Gynec. Obst. **61:** 403, 1935. (3) *Ward, G. Gl:* Surg. Clin. North America **5:** 565, 1925. (4) *Fraenkel, L.:* Ztschr. f. Geburtsh. u. Gynäk. **82:** 59, 1920. (5) *Fraenkel, L.:* Am. J. Obst. & Gynec. **13:** 757, 1927. (6) *Jarcho, J.:* Clin. Med. & Surg. **35:** 555, 1928.

Daly, A.: An Aid in the Treatment of Toxaemias of Pregnancy, J. Obst. & Gynec. Brit. Emp. **40:** 209, 1933.

According to the author, patients with toxemias of pregnancy may be successfully treated by the oral administration of alkaline compound tablets, consisting of potassium citrate, sodium bicarbonate, and calcium sodium lactate. Occasionally it is necessary to give a single intravenous dose of calcium alone. Records of 53 patients so treated are given in tabular form, and a series of 131 patients, treated by routine methods in surrounding hospitals, used as controls. It is claimed that acute cases nearly always show an immediate response to treatment by an increased daily output of urine, a fall in the amount of albuminuria, lowering of hypertension, and a disappearance of edema and other symptoms. The use of an ordinary diet is advantageous. Fetal mortality is diminished because induction of labor is not indicated as often in the tested group as in the controls; 2 per cent versus 66 per cent in the control series. The incidence of spontaneous premature labor is lower in the treated group.

William F. Mengert.

THE MICROSCOPIC AND BACTERIOLOGIC STUDY OF URINE OF OBSTETRIC PATIENTS

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FREQUENT difficulties in correlating clinical evidences of urinary tract infection with the urinary findings led to systematic study of the cytologic and bacteriologic characteristics of the urine in a series of pregnant and puerperal women. Results of this study form the basis of this communication.

METHODS

One hundred and fifty women, admitted consecutively in the last month of pregnancy, and an equal number of puerperal patients were observed on the Obstetric Wards of the University Hospitals. Urine specimens were drawn by catheter at any convenient time during the last month of gestation. Postpartum specimens were similarly obtained during the first ten days after delivery, usually on the ninth or tenth day. The glass catheters were sterilized in mercuric chloride solution and were rinsed in running tap water just before use. The urinary meatus was cleansed with small cotton pledgets soaked in 1:2,000 solution of mercuric chloride. The urine for direct microscopic study was collected in clean, nonsterile bottles, that for bacteriologic study in sterile containers.

For direct microscopic examination, the specimen was centrifuged at uniform, low speed for one minute. A drop of the sediment was placed upon a clean slide and covered with a cover glass. Under the high power, dry lens, at least twenty fields were examined, and the average number of pus cells was recorded. The presence of five or more pus cells in one group was taken to indicate clumping, the incidence of which was recorded as +, ++, +++, or ++++. Note was also made of any bodies which resembled bacteria. A similar preparation was allowed to dry on a slide, was then fixed with heat, and stained by Gram's method. This slide was examined with the oil immersion lens for the presence of bacteria.

The specimens collected in sterile containers were studied by one of us (W. W. H.) without knowledge of the clinical or cytologic findings. Clear specimens were centrifuged at moderate speed (2,000 r.p.m.) for fifteen minutes, and the sediments were plated on the surface of blood agar (sheep defibrinated blood). Specimens showing marked turbidity were plated direct with no attempt at concentration by centrifugation. No quantitative determinations were made nor was any special effort directed toward determining the presence of small numbers of organisms. Bacteria producing colonies on the plates were further identified by their staining reactions and cultural characteristics.

RESULTS

Microscopic examination of the centrifuged, fresh urine gave results recorded in Tables I, II, and III.

TABLE I. PUS CELLS IN THE URINARY SEDIMENT (WET MOUNT)

AVERAGE NUMBER OF PUS CELLS PER HIGH POWER MICROSCOPIC FIELD	ANTEPARTUM PATIENTS		POSTPARTUM PATIENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
None	0	0.0	0	0.0
1 to 5	86	57.3	66	44.0
6 to 10	12	8.0	22	14.7
11 to 15	9	6.0	10	6.7
16 to 25	7	4.7	9	6.0
26 to 50	14	9.3	18	12.0
51 to 100	6	4.0	12	8.0
101 to 200	9	6.0	10	6.7
More than 200	7	4.7	3	2.0
	150	100.0	150	100.0

It is remarkable (Table I) that every urine specimen contained some pus cells, and that in 52 (34.6 per cent) of the antepartum and in 62 (41.4 per cent) of the postpartum specimens, there were more than ten pus cells in the average high power field.

TABLE II. "CLUMPED" PUS CELLS IN THE URINARY SEDIMENT

THE EXTENT OF "CLUMPING"	ANTEPARTUM PATIENTS		POSTPARTUM PATIENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
None	114	76.0	100	66.6
+	14	9.3	21	14.0
++	13	8.7	18	12.0
+++	5	3.3	6	4.0
++++	4	2.7	5	3.3
	150	100.0	150	100.0

Considerable "clumping" (more than +) was noted in 22 (14.7 per cent) of the antepartum and in 29 (19.3 per cent) of the postpartum urines. It is evident that many individuals in both groups, who showed a considerable number of pus cells in the urine, did not present the "clumping" phenomenon. On the other hand, it is surprising that such a large percentage presented "clumped" pus cells, a finding which is commonly associated with clinical urinary tract infection.

TABLE III. BACTERIA IN FRESH URINARY SEDIMENT (WET MOUNT)

RELATIVE NUMBER OF VISIBLE BACTERIA	ANTEPARTUM PATIENTS		POSTPARTUM PATIENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
None	20	13.3	14	9.3
+	65	43.3	72	48.0
++	28	18.7	30	20.0
+++	16	10.7	13	8.7
++++	21	14.0	21	14.0

Sixty-five (43.4 per cent) of the antepartum and 64 (42.7 per cent) of the postpartum specimens showed considerable numbers of bacteria on direct examination (wet mount). These figures parallel closely

the number of specimens with more than 10 pus cells per high power field (Table I). Although bacteria were detected usually in direct examination of the urine which showed numerous pus cells, such was not invariably the case.

TABLE IV. BACTERIA IN STAINED (GRAM'S TECHNIC) URINARY SEDIMENT

TYPES OF ORGANISMS	ANTEPARTUM PATIENTS		POSTPARTUM PATIENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
None	39	26.0	9	6.0
Gram-negative bacilli only	52	34.7	60	40.0
Gram-negative bacilli with gram-positive cocci	35	23.3	50	33.3
Other organisms	24	16.0	31	20.7
	150	100.0	150	100.0

It is to be noted that relatively few (26 per cent of antepartum and 6 per cent of postpartum) urine specimens were bacteria-free, as shown by the stained preparations. It was anticipated, from the knowledge of frequent urinary tract invasion by the colon bacillus, that gram-negative rods would likely predominate. However, the results obtained by culture (Table V) indicate that comparatively few of the types of organisms belong to this group. No particular effort was made to identify those organisms not of the colon group, as it had been considered that only the latter are commonly associated with clinical infection.

TABLE V

ORGANISMS	ANTEPARTUM PATIENTS		POSTPARTUM PATIENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
No growth	32	21.2	22	14.7
Escherichia coli	9	6.0	8	5.3
E. communior	4	2.7	9	6.0
Alcaligenes fecalis	6	4.0	5	3.3
Bacillus subtilis	6	4.0	6	4.0
Staphylococcus albus	12	8.0	20	13.3
Monilia	7	4.7	1	0.7
Gram-positive rods	16	10.7	7	4.7
Miscellaneous	58	38.7	72	48.0
	150	100.0	150	100.0

Cultures indicate a greater number of specimens to be bacteria-free, as measured in terms of ability to grow and form colonies, than is shown by the study of stained slides of urinary sediment. Both methods, however, demonstrate that very few of these specimens, even though obtained by catheterization, were sterile. The presence of certain organisms, *Staphylococcus albus* and *Bacillus subtilis*, suggest contamination during or after catheterization, while some of the unidentified, gram-positive rods may have been the vaginal bacilli of Döderlein.

It is apparent (Table VI) that increased numbers of cells per high power field were, in general, paralleled by a greater incidence of

pyelitis, but 27 per cent of antepartum and 24 per cent of postpartum women with marked pyuria (more than 50 pus cells per field) had no associated clinical evidence of pyelitis. Also, 5 of the 10 patients showing 200 or more pus cells per field were free of urinary symptoms, whereas one antepartum woman had symptoms of pyelitis with less than 5 cells per field.

TABLE VI. THE RELATION OF PYURIA TO CLINICAL MANIFESTATIONS

AVERAGE NUMBER OF PUS CELLS PER HIGH POWER MICROSCOPIC FIELD	ANTEPARTUM PATIENTS			POSTPARTUM PATIENTS				
	NO. OF CASES	PYELITIS		NO. OF CASES	PYELITIS		FEBRILE PUERPERIUM	
		NO.	PER CENT		NO.	PER CENT	NO.	PER CENT
0 to 5	86	1	1.2	66	0	0.0	13	19.7
6 to 10	12	0	0.0	22	0	0.0	2	9.1
11 to 25	16	0	0.0	19	1	5.3	4	22.2
26 to 50	14	2	14.3	18	0	0.0	3	16.7
51 to 100	6	1	16.7	12	3	25.0	3	25.0
101 to 200	9	2	22.2	10	1	10.0	3	30.0
More than 200	7	3	42.9	3	2	66.7	2	66.7
	150	9	6.0	150	7	4.7	30	20.0

DISCUSSION

These data indicate that moderate numbers of pus cells are a normal finding in the urine of women during late pregnancy and the early puerperium. Pyuria, then, does not necessarily mean that the patient has pyelitis, nor does its absence eliminate the diagnosis of this clinical entity. It is possible that the pain and tenderness over the kidney region in patients with pyelitis are due to distention of the renal pelvis, and that this may or may not result in the exudation of polymorphonuclear cells into the urinary tract. The function of this tract, having thus been interfered with by the distention producing factor, may become secondarily invaded by a number of organisms. These latter may then be considered incidental to the essential lesion, but may contribute somewhat to the disturbance of function. An analogous condition is found in the secondary invasion of the bladder by bacteria when there is some interference with normal emptying. If this is accepted, it is apparent that the chief distinctive evidence of urinary tract infection is the discomfort incident to the accompanying cystitis and to the fever with chills.

CONCLUSIONS

1. Bacteria and pus cells are present in the urine of practically all late pregnant and early puerperal women but are without clinical significance in themselves.

2. The diagnosis of pyelitis must rest on symptomatology and may or may not be accompanied by pyuria and bacteriuria.

CERVICITIS AND ENDOCERVICITIS IN RELATION TO GYNECOLOGIC SYMPTOMATOLOGY*

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THE consideration of cervicitis and endocervicitis probably seems a very elementary problem. However, when one constantly sees patient after patient presenting themselves for relief of various gynecologic complaints, and have been advised to have major surgical procedures done for the relief of these symptoms, one is inclined to stop and wonder if we are not frequently overlooking a very simple and common cause of these complaints, namely, inflammatory lesions of the cervix and endocervix.

Cervicitis and endocervicitis are such extremely common conditions that we are inclined to disregard their major importance in gynecologic symptomatology. Briefly, reviewing the etiology of cervicitis and endocervicitis, we find that it is most often found in women who have had one or more children with resulting lacerations in the cervix, permitting easy access of bacteria into the cervical canal. It is not at all uncommon, however, in nulliparous women, young girls, and even in infants. It is a question whether the cervix ever escapes contamination in ascending infections of the genital tract. Infection once implanted on the cervical mucous membrane may endure for an indefinite period of time due to the anatomical construction of the endocervix, particularly because of the folds of the cervical mucosa and presence of compound racemose glands. Infections in this region may be deep seated, which fact explains the difficulty in curing these lesions and the tendency to chronicity. Inflammatory reaction and infection of the cervix is usually brought about by lacerations, exposure to sex trauma, instrumentation, and its being constantly bathed in bacteria of one type or another, thus introducing the infection into the cervical canal. As a result of these infections numerous symptoms may develop depending upon the severity and extent of invasion and involvement of the reproductive organs.

Leucorrhea is probably the most common symptom resulting from bacterial invasion of the endocervical glands. This discharge may in turn produce changes in the vulva not unlike that seen in diabetes, leucoplakia, and kraurosis vulvae. The associated symptoms are those of burning, intense itching, smarting on urination, and dyspareunia.

*Read at a meeting of the Chicago Gynecological Society, January 17, 1936.

Similar symptoms may be produced by a vaginitis as a result of various organisms, the most common of which are *Trichomonas vaginalis,* streptococci, yeast and fungoid infections, all of which may have an associated cervical infection. Satisfactory results in the treatment of many of these cases are not obtained until the cervical infection is eliminated. In infants and young girls the discharge and vaginitis produced by endocervicitis and cervical erosions are not infrequently mistaken for a specific infection. Cervical lesions causing leucorrhea are also one of the most common causes of relative sterility, mainly, by blocking the entrance of sperms into the uterine cavity. It may also change the character of the bacterial flora and conditions in the vagina which either actively prohibit the motility of the sperms or noticeably retard their activity.

The cervix is richly supplied with lymphatics which combine with the lymphatics of the upper part of the vagina and drain into the iliac glands. This may produce marked induration of the uterosacral ligaments causing them to be extremely swollen and tender, producing pain and backache in the sacral and lumbosacral regions. This backache may be in part reproduced by touching the inflamed cervix with a strong chemical irritant such as tincture of iodine or silver nitrate. Many times the patient will say that this procedure reproduces the exact pain for which she presents herself for relief. The pain can also be reproduced by pushing the cervix anteriorly, putting the uterosacral ligaments on a stretch. Induration and tenderness of the uterosacral ligaments also often produce dyspareunia.

Burning on urination, urgency, and bladder tenesmus are occasionally found to be relieved by clearing up an existing cervical lesion. Whether these bladder symptoms are due to direct infection through the urethra or by lymphatic drainage is problematical.

There are many patients who present themselves with symptoms of sacroiliac arthritis or subluxation, which promptly disappear after clearing up any existing cervical infection. As evidence of this I would like to present a typical case history.

Mrs. H., aged twenty-eight, came in to see me June 10, 1935, because of an irritating profuse leucorrhea which she had had since the birth of her child eighteen months previously. She also complained of dyspareunia and a severe sacral backache during this time which had been diagnosed as sacroiliac arthritis for which she had had a tonsillectomy done and two teeth extracted. She was told that she had a retroverted uterus that would need surgical correction. She also had been under the care of an orthopedic surgeon who prescribed a body cast which she had worn for about six months, removing it temporarily for physiotherapy and massage. None of the foregoing management had given relief. On examination the patient had a moderate cystocele and rectocele. There was a profuse mucopurulent discharge in which no *Trichomonas vaginalis* could be found. The cervix was edematous, lacerated bilaterally, badly eroded and contained several infected nabothian cysts. There was marked induration and tenderness of both uterosacral ligaments. The uterus was retroverted, enlarged, and tender on motion, no abnormal masses could be

felt in the region of either adnexa. Pushing the cervix anteriorly reproduced the pain in the back, of which she complained. The cervix was cauterized on three different occasions, the nabothian cysts destroyed with the fine pointed cautery. At her last visit November 5, there was no leucorrhea, the cervix was clean, uterus in normal position, and she was free of all backache and pelvic discomfort.

The increased size and bogginess of the uterus due to inflammatory lesions of the cervix is frequently the cause of retrodisplacements, the uterus falling back because of its increased size and weight. On the other hand, there are many cases of retroverted uteri producing symptoms of pressure in the pelvis, backache, dysmenorrhea, dyspareunia, and leucorrhea that are thought to be due to the position of the uterus. These symptoms often disappear after existing cervical lesions are cured, even though the uterus remains retroverted, thus proving that it was not the retroversion that was causing the trouble but the associated cervical infection. These retrodisplacements may spontaneously return to normal position when the existing cervical infection is relieved. This is particularly true of retroverted uterus with cervical lesions following childbirth.

There is some argument as to whether cervicitis and endocervicitis can act as a focus of infection. There are some who claim that this is true and that an infected cervix is analogous to the tonsils, teeth, or other foci. There are others who say that infections in the cervix never act as a general systemic foci, causing arthritis, neuritis, neuralgia, etc., except gonorrheal infections which may cause gonorrheal arthritis. However, it is not inconceivable that some cervical infections may be related to general systemic or rheumatoid conditions.

Endocervicitis, cervicitis, erosion, ectropion and polypus formation all are related conditions and may represent different stages of the same process. Erosion, ectropion and cervical polyps may, and frequently do, produce contact bleeding and metrorrhagia not unlike that seen in malignancy. The appearance is frequently very similar and cannot easily be differentiated. Senile atrophy sometimes predisposes the endocervix to infection producing partial or complete atresia. The result may be the backing up of infection in the uterine canal, producing a pyometra which is thought to be an etiologic factor in the production of malignancy of the corpus.

Severe dysmenorrhea may also be an associated symptom especially when an erosion is present. Many women have had a dilatation and curettement done for dysmenorrhea with no relief until existing cervical lesions are eradicated.

Menorrhagia or increased duration and quantity of menstrual flow, not infrequently mistaken for that caused by fibromyoma uteri, is in reality often the result of an inflammatory process secondary to cervicitis and endocervicitis.

As an example of this I would like to present another case history. Mrs. K., aged forty-three, presented herself Sept. 26, 1932, complaining of pain and dragging sensation over the right inguinal region, profuse menstrual periods, lumbosacral backache, and severe dysmenorrhea. Menstrual history: Onset at twelve, regular, twenty-eight-day interval lasting three or four days, with use of 6 or 8 napkins during the period, and no pain. For the last year the periods had gradually come to last seven or eight days and become more profuse, requiring 18 to 24 napkins, with pain lasting throughout the entire period and much generalized discomfort. During this time she also had noticed a moderately profuse vaginal discharge. She had one miscarriage, two children the youngest being 14 years. Vaginal examination revealed a moderate cystocele and rectocele. The cervix was lacerated bilaterally, edematous, filled with nabothian cysts and badly eroded. The uteral sacral ligaments were tender and indurated. The uterus was in normal position about the size of a small orange, boggy in character except for a fibroid nodule in the right horn about the size of a large English walnut. The patient was told that her difficulty might be in part caused by the infected lacerated cervix and in part by the fibromyoma. She was advised to have the cervix cleaned up before any operative procedure that might be necessary. I did not see the patient again for about two months during which time she had visited one of the better clinics where she was told that she had a fibroid the size of a grapefruit and an immediate hysterectomy was advised. She again presented herself for attention and the cervix was cauterized on four different occasions. At the time of her last visit, Sept. 3, 1935, the uterus was definitely smaller in size. The fibroid had not increased in size and she was free from backache, dysmenorrhea, and leucorrhea. The last three periods had been at twenty-eight-day intervals, lasted three or four days and required 8 or 9 napkins during the entire period. This case proves beyond question that the cervical lesion was responsible for her complaints rather than the existing fibromyomas.

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DISCUSSION

H. O. MARYAN.—I wish to report the results of 32 cases of urinary disturbance due to chronic cervicitis. This work was done in collaboration with Drs. Russel Herrold and E. Ewert of the Urological Department of the University of Illinois. The method of treatment in all these cases was electrical coagulation by means of the crucial incision and striping method.

These women generally complain of frequency of urination with burning before and after, intermittent deep pain above the pubis, low backache, and less frequently, radiating pains into the groin, the thigh, and upward along the course of the ureter. This syndrome is frequently designated as the irritable bladder, some believing the urine to be bacteria free. Many of these patients have pronounced leucorrhea.

DR. HOLLOWAY (closing).—I have had two patients with persistent bladder symptoms in spite of a urine in which pus was never noted. Urethral polyps were found and removed but the symptoms continued. The patients subsequently became symptom free after cauterization of the cervix.

Some of these cervical glands may extend up to the uterine body. Cauterization to the level of the internal os would not, therefore, remove all the potentially infectious gland tissue.

SYMPTOMATIC RUPTURE OF THE GRAAFIAN FOLLICLE OR CORPUS LUTEUM

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THE rupture of a graafian follicle and the development of the corpus luteum, although usually unattended by untoward symptoms, may on occasion be the cause of severe abdominal complaints. The condition is seldom recognized before operation since the symptoms closely resemble those produced by other pelvic or gastrointestinal diseases.

A review of the literature by Morton[1] in 1932 revealed 93 authentic cases. Since then additional cases have been added to bring the number well over one hundred.[2-4] Most reported cases present marked and sometimes alarming symptoms of severe hemorrhage from the follicular apparatus. These are characterized by severe sudden pain, which is likely to be lower abdominal at first, but which may later become generalized, and also by evidence of hemorrhage, such as rise in pulse, fall in blood pressure, pallor, faintness, nausea, and /or vomiting.

More recently Pratt[5] placed emphasis upon the development of mild or moderate symptoms associated with ovulation and the formation of the corpus luteum when there was little or no hemorrhage from the ovary. He pointed out that a thorough familiarity with these symptoms is essential in differentiating between this condition and appendicitis.

From the material available at the University Hospital and the Chicago Lying-In Hospital, we are able to analyze 17 cases and the findings are summarized here.

The youngest patient was seventeen and the oldest forty years of age, with an average age of twenty-six years. There were 7 multiparas and 10 nulliparas. Fifteen of the patients gave a normal and regular menstrual history while one patient menstruated every six to eight weeks, and one, although presenting well-developed secondary sex characteristics, had never menstruated.

Pain was the only constant symptom in all cases and was the first symptom in each. Its severity varied from a mild, dull ache to very severe pain causing fainting. In every instance the onset was sudden. Eight patients had pain only in the right lower quadrant, 3 in the left lower quadrant, and 6 complained of generalized lower abodminal pain. Eight complained of nausea and vomiting, while the remaining 9 had no gastrointestinal symptoms. In previous reports trauma has been mentioned as an important etiologic factor. In this group there was a record of trauma in only 2 cases. One patient developed symptoms immediately after a vaginal examination and the other during rather strenuous exertion (running).

The time of onset of the symptoms in relation to the cycle is of interest in differentiating between follicular and corpus luteum hemorrhage (Table I). Five of the patients developed their symptoms from thirteen to fifteen days after onset of the previous period. Material for microscopic study was available in 4, and, in all, revealed only cystic follicles with hemorrhage. The other patient was treated con-

servatively and was discharged in three days. Ten patients developed symptoms later than three weeks after the previous period. Pathologic material from these showed large corpora lutea with hemorrhage. The other 2 patients had irregular and atypical menstruation, and the time of onset in relation to the period was questionable, but in each it was more than three weeks after the previous period. Both of these patients were found to have hemorrhage from a corpus luteum.

Physical examination in this group of patients gave very few consistent findings. Lower abdominal tenderness either general or limited to one of the lower quadrants and of varying severity was present in all cases. Muscle spasm over the side involved was present in about one-half of the cases. Three patients did not have a pelvic examination. Pelvic examination in the remainder revealed tenderness on manipulation of the uterus in all cases. A definite mass was felt in the region of the involved appendage in 5 cases. In 4 an indefinite mass was noted, while in 5 no mass could be palpated.

TABLE I. ONSET OF SYMPTOMS IN RELATION TO CYCLE

MENSTRUAL PHASE	PROLIFERATIVE PHASE	OVULATION TWELFTH TO SIXTEENTH DAY	PREMENSTRUAL PHASE
1-1 Day after onset		2-13 Days postmenstrual	1-21 Days postmenstrual
1-3 Days after onset		3-14 Days postmenstrual	1-22 Days postmenstrual
			2-27 Days postmenstrual
			2-28 Days postmenstrual
			1-29 Days postmenstrual
All showed hemorrhage from corpus luteum		All showed hemorrhage from graafian follicle	All showed hemorrhage from corpus luteum

Two cases with grossly irregular menstrual history had hemorrhage from a corpus luteum. One patient treated conservatively. Pathologic material not available for study.

The temperature varied from normal to 101°. The higher fevers occurred in the patients with higher leucocyte counts. The pulse was slightly elevated in about one-half of the cases, with an average pulse rate of 88.

The leucocyte count varied from 5,400 to 22,650. The degree of reaction in the blood corresponded roughly to the time interval between the hemorrhage and the examination, and to the amount of organization of the hematoma which had taken place, i.e., the lowest counts were in those patients with fluid blood or follicular fluid in the abdomen who were seen a few hours to one or two days after the onset of symptoms. The higher counts occurred in those patients seen a week or more after onset. The count of 22,650 was in a patient whose symptoms had persisted for five weeks.

The original diagnoses (made when the patients were first seen) were as follows: In 5 the diagnosis was ectopic pregnancy. Seven were diagnosed appendicitis, 1 a hydrosalpinx, and 1, the patient with total primary amenorrhea, was thought to have an ovarian neoplasm with some degenerative change. Three patients were diagnosed as ruptured follicle with hemorrhage, and in one of the cases which was diagnosed as appendicitis, the possibility of rupture of follicle with hemorrhage was mentioned. One of the patients with the original diagnosis of ruptured follicle was not operated upon, but in view of the convalescence and future course, we felt justified in including the case in this report.

At the time of operation 15 of the 16 patients showed gross blood in various stages of organization. The other patient presented a rent in the surface of the right ovary with a small hematoma in the follicle and a small amount of clear fluid in the culdesac. The occurrence of symptoms in the presence of gross hemorrhage is understandable. The presence of symptoms in the one case without hemorrhage, however, leads us to agree with Pratt that the rupture of the follicle with discharge of follicular fluid is capable of producing sufficient peritoneal irrita-

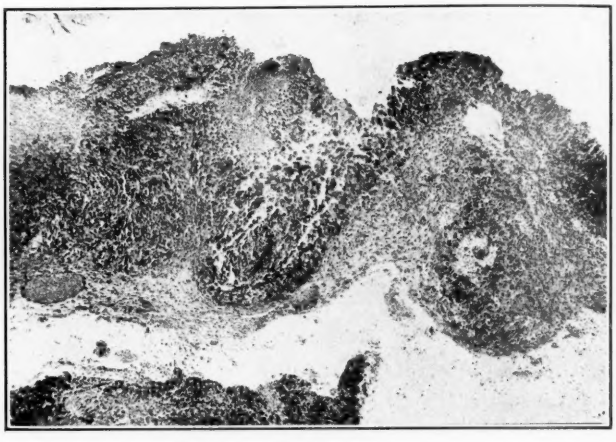

Fig. 1.—Photomicrograph from case of follicular rupture with hemorrhage showing granulosa cells, ovarian stroma and extravasated blood. (×65)

Fig. 2.—Photomicrograph from case of corpus luteum hemorrhage showing lutein cells, ovarian stroma and hemorrhage. (×63)

tion to cause clinical symptoms, and has caused us to be more careful when investigating female patients with symptoms of acute appendicitis.

The differentiation cannot always be made but a consideration of the salient points will be helpful. The onset of the pain in follicular rupture usually is more sudden and sharp and starts over the area involved. Nausea and vomiting are less pronounced; temperature and leucocyte count are usually lower. The localization of tenderness is below McBurney's point (Table II).

TABLE II. DIFFERENTIAL DIAGNOSIS

SYMPTOMS	APPENDICITIS	FOLLICULAR RUPTURE
Pain	Starts in epigastrium then localizes in the R.L.Q.	More sudden and severe. Starts over involved appendage
Tenderness	Maximum at McBurney's point	Maximum apt to be below McBurney's point if in right side
Leucocytes	10,000-15,000	Normal or only slightly elevated in mild cases
Fever	Normal—101	Seldom over 100°
Nausea and vomiting	The rule	Less common except in more severe cases
Menstruation	No definite relation to cycle	Variable but usually either at time of ovulation or premenstrual or early menstrual phase

The question of operation should depend on evidence noted in each case. In any event, operation is indicated regardless of the differential diagnosis when symptoms indicate a major abdominal crisis.

SUMMARY

The sudden onset of lower abdominal pain in any woman at the time when ovulation should occur (twelve to sixteen days postmenstrual) or shortly before the onset of menstruation, with or without slight fever and leucocytosis, suggests the diagnosis of ruptured graafian follicle or corpus luteum. The severity of the symptoms should be the guide in regard to operation. If mild, observation for a few hours with frequent check of the fever and leucocyte count and close observation of the patient for evidence of progressive hemorrhage is indicated. If the possibility of appendicitis cannot be satisfactorily ruled out and operation is decided upon, we favor the use of a median or paramedian incision to permit adequate exploration of the pelvic viscera.

The treatment of the ovary at the time of operation will depend entirely upon the amount of pathologic change present. In the case of a small rent with mild hemorrhage, suture of the opening is adequate. In the presence of larger hematoma partial resection of the ovary may be necessary, and when the whole appendage is involved with organizing hematoma, it may be wise to remove completely the involved tube and ovary.

REFERENCES

(1) *Morton, P. C.:* New York State J. M. **32:** 196, 1932. (2) *Meigs, J. V., and Hoyt, W. F.:* AM. J. OBST. & GYNEC. **25:** 532, 1933. (3) *Allen, A. D., and Gamble, W. G.:* J. Michigan M. Soc. **33:** 139, 1934. (4) *Hewitt, H. W., and Slevin, J. G.:* J. Michigan M. Soc. 32: 445, 1933. (5) *Pratt, J. P.:* AM. J. OBST. & GYNEC. **27:** 816, 1934.

DÜHRSSEN'S INCISIONS*

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INCISION of the cervix as an aid to delivery is on record as early as the eighteenth century, but it was Dührssen who showed the value of these incisions so conclusively. The usefulness of this operation is limited to some extent because incision is safe only after effacement of the cervix. Dührssen proposed deep lateral incisions and if not sufficient, anterior and posterior as well. Recent reports on the use of cervical incisions indicate that at present they mostly are made in the oblique diameters, which seem to be preferable. Available records indicate that these incisions are used as a last resort after long difficult labors without advancement of the head.

I am not advocating anything new as to procedure, which is very simple, but I am pleading for more frequent use of the incisions in definitely indicated conditions, which I shall take up later.

Shir† in a rather apologetic manner states that he does not wish to be understood as advocating frequent Dührssen's incisions of the cervix. Quite to the contrary he looks upon it as a major operation to be resorted to but rarely though there is a definite field for its occasional use. He feels that conservative waiting beyond a certain point is no longer a virtue.

Shir reports the type of case known to all obstetricians. Labor goes on hour after hour, sometimes several days; finally the cervix disappears, the occiput rotates, and the baby may be delivered. These patients, however, later show a deep bilateral laceration of the cervix into the vault of the vagina. What has taken place is not dilatation at all, but gradual edema and loss of elasticity of the cervix with finally spontaneous laceration. I readily agree with Shir when he states that to push the cervix back over the head is simply to lacerate it instead of incising it. His records show that incisions were made once in every 161 cases. The average stay in the hospital was 15.8 days in spite of the fact that labor usually lasted over two days, showing that morbidity was not great. This operation was resorted to in his series only after a long labor when the patient was already infected and worn out, and the baby was in grave danger. Twenty-seven of these 143 babies were lost, 6 of these were dead before interference was attempted.

*Read at the Seventh Annual Meeting of the Central Association of Obstetricians and Gynecologists, held at Omaha, Neb., October 10 to 12, 1935.

†Am. J. Obst. & Gynec. 26: 425, 1936.

Such figures might indicate that Dührssen's method is risky and objectionable. However, I desire to show that had Dührssen's method been applied earlier in labor many of these babies might have been saved.

Caldwell, in Curtis' *Obstetrics and Gynecology,* states that attempts to deliver through the obstructed cervix without incision leads to spasms of the lower uterine segment, and that many of these patients can be delivered easily after cervical incision, saving the baby and leaving the mother in a better condition. Incisions are more easily repaired and heal better than ragged tears.

Given a fairly normal pelvis and a child not out of proportion, the most frequent cause of delayed difficult delivery is the occipitoposterior position. Fetal mortality and maternal injury and morbidity in these cases is still too high. Many methods have been advocated for their management. Although it is recognized that various types of pelvic disproportion are causes of occipitoposterior positions, there are many cases which are not explained by abnormal pelves. The etiologic factor here probably lies in the uterus or the cervix. It is usually in this type of case, where advancement and rotation fails to take place and the cervix does not dilate beyond four fingers, that I advocate more frequent and earlier use of incisions of the cervix. Although incisions may help in some of these other cases, I do not consider it justifiable to employ them as frequently as with the normal pelvis, since other factors must first be evaluated. The by-word of all obstetrics is watchful expectancy, in other words, as far as possible, conservatism. When progress is definite and mother and baby are in good condition, I am sure everyone agrees that this is by far the best policy. However, in the type of cases under discussion, where the cervix does not dilate properly and progressively, but with the continuation of labor the edges become thicker and more edematous, I have obtained by far the best end-results as to both mother and child by what might be considered a radical procedure but which I believe to be conservative.

In going over my records and examining the patients for end-results I have found that those patients who were allowed to labor for many hours, with a thick cervical rim, almost invariably showed deep bilateral lacerations, frequently into the vault of the vagina. After patient waiting we suddenly find that we seemingly have been rewarded and the baby is born. The end-results prove that this was not a conservative procedure, as the fetal mortality is high and maternal damage is great. On the other hand, in this type of case where the cervix dilates to three or four fingers and remains stationary for two

or three hours, the head failing to advance or to rotate, incisions usually terminate labor very quickly with both the baby and the mother in better condition.

I have found that in the majority of these cases two incisions in the position of ten and two on the clock are sufficient if the incisions are made at least 1½ to 2 inches long. The surprising feature is the exceedingly small amount of bleeding; often no blood loss at all being encountered, probably because of the extreme edema and anemia of the cervix at the time of incision.

Repair of the cervix is exceedingly simple even without special retractors, as the cervix can easily be pulled down with sponge forceps. Two interrupted sutures, as a rule, in each incision is all that is necessary. The follow-up after six or eight weeks has shown normal appearing cervices, sometimes requiring close search for the scar of the incision.

Although I realize that this series consisting of 36 cases is small, the results have been so entirely satisfactory that I feel I can draw some definite conclusions. In fact, the corrected fetal mortality of this series is zero. There were three dead babies. Two of them were cases of craniotomies for hydrocephalic and exceedingly large babies, their heads being almost the size of watermelons. The other death was that of a 1,600 gm. baby with multiple anomalies, born alive, dying later. A few case reports follow to show the types of labor with the results, which allow me to draw my conclusions.

The first few cases of the series showed a longer labor than did the cases of the last few months. In these I have taken a more positive stand and have terminated labor earlier when dilatation and advancement of the head had apparently ceased.

The first case of this series occurred about four years ago. This primipara entered the hospital with ruptured membranes, contractions every two minutes, of sixty to seventy seconds' duration. Position was R O.P. and the cervix effaced and one finger dilated. Dilatation was rather slow from the start, and after seven hours of labor in the hospital, she had only two and one-half fingers' dilatation. Fourteen hours later she had three fingers' dilatation with the head still in midpelvis and the occiput posterior. Three hours later this patient had four and one-half fingers' dilatation. This was after a labor of almost twenty-four hours. Four hours later this patient still had four and one-half fingers' dilatation, the head was still in midpelvis and the anterior lip was becoming markedly edematous. Two hours later as conditions were still the same, the patient was given an anesthetic and Dührssen's incisions were made in the position of ten and two on the clock. Midforceps Scanzoni maneuver was done without difficulty and the patient delivered after an episiotomy. Repair of the cervix was accomplished with two interrupted No. 1, twenty-day catgut sutures on each side. The perineum was repaired and the postpartum course was normal. This labor lasted over thirty hours with a baby weighing only 2,550 gm. and with a normal pelvis. Examination of the cervix six

weeks later showed it to be normal without eversion and genitalia in good condition. Delay of labor in this case was due primarily to the cervix and the posterior position was secondary.

There were three cases of breech presentation in this series which were delivered without difficulty after Dührssen's incisions were made. All were primiparas. Two of them showed no progress after four to four and one-half fingers' dilatation with the breech in midpelvis, contractions being good. The first patient was allowed to labor ten hours without progress before incisions were made. The second case was delivered following incision of the cervix when labor showed no progress after four hours. The third patient had one finger dilatation on entrance to the hospital. Labor was satisfactory and progressive with four fingers' dilatation six hours later. At this time the membranes ruptured spontaneously and on examination a prolapsed cord was found. Fetal heartbeat was 80 per minute. A living baby was delivered here also following Dührssen's method. All of these patients had three incisions as I wished to be certain that the cervix would not interfere in any way with the aftercoming head.

There was one case of twins in a very small woman, weighing 91 pounds when she first came to see me and 124 pounds at the time of delivery. McDonald measurement was 46 cm. The abdomen was so large that the labor pains although frequent and of good quality were ineffectual. Although pains were almost continuous for about four hours before the patient was placed on the delivery table, there was no progress in dilatation. Examination revealed four fingers' dilatation from 7:30 P.M. to 11:50 P.M. At this time two incisions were made in the cervix, the anterior lip of which was becoming edematous, and both babies delivered without difficulty. Delay in these cases was probably due to insufficient uterine force.

Twenty-eight patients of this series were primiparas and eight were multiparas.

One multipara had a three-hour labor with the first baby and no difficulty. With this second child the position was R. O. P., pains good, every two minutes, of sixty to seventy seconds' duration. This patient had four fingers' dilatation after twelve hours in the hospital with hard contractions. Two hours later there was still four fingers' dilatation and the membranes were ruptured artificially. Three hours later, with good cooperation from the patient there was no further advancement and the anterior lip was very edematous. The patient was tired. She was placed on the delivery table and two Dührssen's incisions were made. Four minutes later after two contractions the head was found on the pelvic floor and delivered with perineal forceps.

Two other patients, primiparas, were allowed to deliver spontaneously after the incisions were made. These patients had been in active labor for several hours without progress after four fingers' dilatation. The head could be seen to rotate and descend with the first pain after the incisions. These patients both delivered spontaneously without difficulty. These cases proved to me that occiput posterior was secondary and the cervix primary.

The two patients with hydrocephalic babies, both primiparas, had labors somewhat similar, lasting more than forty-eight hours, with irregular ineffectual contractions. Dilatation was two fingers at this time, and a bag was inserted into the cervix. The bag was expelled after several hours with about four fingers' dilatation. Contractions again became irregular and the cervices contracted down to about two and one-half fingers. During this time the patients had been given morphine and hyoscine at intervals, as well as intravenous glucose. As there was complete effacement, three Dührssen's incisions were made, and the babies were delivered after craniotomy.

One patient in this series had Dührssen's incisions for both deliveries, both labors being similar with primary inertia and no progress after about three fingers' dilatation. Two other primiparas who had Dührssen's incisions with the first delivery have since been delivered spontaneously after short normal labors.

At the present time after observing these patients and comparing them with other cases of retarded labor, I feel very definitely that it is not a radical procedure to make these incisions in the cervix, when after three or four hours of good labor there is no advance of the head or appreciable increase in dilatation of the cervix. There was no maternal mortality and the morbidity was no higher than that following normal cases. The end-results have been consistently good. On the other hand, in patients in whom the policy of watchful expectancy had been followed, the cervices showed deep bilateral lacerations and the end-results were not so good. The total number of deliveries during the four-year period of this report was 583; or 6 per cent had Dührssen's incisions.

CONCLUSION

1. The performance of Dührssen's incisions is a safe and simple operation but must be done after complete effacement when the vessels and bladder are well retracted. If there is no effacement, Dührssen's incisions should not be done.

2. The type of case in which this operation is most satisfactory is the one in which the patient has been allowed to go spontaneously into labor because of normal pelvic measurements, and in whom the progress is not satisfactory because of malposition or inertia or abnormality of the cervix, and particularly, where the membranes have been ruptured, when it would be more hazardous to attempt cesarean section.

3. I am not suggesting any change in Dührssen's method but I am advocating a much earlier and more frequent use of the method in properly selected cases, as I am certain that it is the means of saving many babies who would otherwise be lost.

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Vayrynen, V.: Cases of Polyneuritis and Myelitis Caused by the Toxemias of Pregnancy, Acta obst. et gynec. Scandinav. **15**: 182, 1935.

The author reports 5 personal cases of myelitis and polyneuritis caused by the toxemias of pregnancy. The clinical picture of these cases was the same as it is for these diseases in the nonpregnant state. The disease usually begins as ordinary vomiting of pregnancy. It soon becomes excessive vomiting. Hence, in all patients who have hyperemesis gravidarum the nervous system should be carefully investigated. Because of the high mortality (42 per cent), the author advises interruption of pregnancy as soon as any signs of paralysis appear.

J. P. Greenhill.

TRIPLE PREGNANCY DIAGNOSED BY MEANS OF X-RAY

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A CAREFUL search of the available literature reveals only 9 cases in which the diagnosis of triplets was made before delivery. H. Marcus[1] reviewed the literature in 1928 and found 4 cases to which he added a fifth. To briefly summarize Marcus' report: Edling[2] reported a case in 1911 in which the diagnosis of twins was made by x-ray at the fourth month. The patient delivered triplets and, upon reexamining the plates, shadows which were not noted before delivery were interpreted as being those of the third fetus. Essen-Möller[3] in 1920 had a patient delivering triplets on whom an x-ray examination was made before delivery but after she had started into labor. The diagnosis was made at the time of delivery before the result of the examination was known. Favreau and Despons[4] in 1924 made a diagnosis of triplets by x-ray at the sixth month. Genell[5] in 1926 diagnosed a triple pregnancy by the visibility of 3 vertebral columns on the x-ray film. Marcus' patient was a primigravida, twenty-nine years old, who was first seen about two weeks before the expected date of confinement. Her abdomen was very large, and it was difficult to make an exact examination because of the tenseness of the abdominal wall. There were 2 resistant surfaces felt which gave the impression of backs. A fetal heart could be heard distinctly at one point. When the patient returned one week later, examination by palpation was no more satisfactory than at the first visit, and it was decided to make an x-ray examination. The membranes ruptured spontaneously the same evening and she started into labor. The results of the x-ray examination were made known during the course of labor and indicated a triple pregnancy. Two of the fetuses were well developed, but the bones of the third seemed to be lying in an irregular-shaped mass, indicating that the fetus was dead and macerated. The accuracy of the radiologic diagnosis was confirmed at delivery.

Dr. Robert A. Johnston[6] also, in 1925, reported a case of triplets diagnosed by x-ray two months before delivery. Two fetal hearts had been heard but a definite diagnosis by palpation was not possible. The patient was delivered approximately at term of 3 living children. A recent letter from Dr. Johnston states that they are still living and in excellent health.

There were 2 cases reported in 1930. Dr. Leo A. Rowden[7] reported the diagnosis of triplets by means of the x-ray one month before delivery. The patient was delivered of 3 healthy male infants at the seventh month. The writer makes the statement that he has not seen another case in the English literature. Trillat, Eparvier, and Naussac[8] reported the case of a thirty-year-old primigravida who was first seen at term. The abdomen was very large, measuring 44 cm. vertically. The first examination indicated a twin pregnancy but repeated examinations revealed a mass just below the umbilicus which might have been a fetal head. An x-ray examination showed the presence of 3 fetuses. The authors stressed the fact that a correct diagnosis could have been made only by x-ray, as diagnosis by palpation alone was impossible. The labor was long with mild infrequent pains. Delivery was completed under general anesthesia and 3 living infants were extracted. All 3 children lived.

The ninth case was reported by Dr. Albert H. Aldridge[9] in 1932. The diagnosis was made three weeks before the expected date of confinement by means of the x-ray.

All 3 babies were breech presentations. The patient went into labor two days later and delivered the first baby spontaneously at the end of the second hour. The other 2 babies were easily delivered. The delivery was uncomplicated, except that immediately postpartum the patient had a rapid rise in pulse rate to around 200 per minute. It fell abruptly after twenty-five minutes to 80 per minute and remained normal. The puerperium was uneventful. All 3 babies were males and were born alive; their weights were 4 pounds 7 ounces, 4 pounds 3 ounces, and 3 pounds 3½ ounces, respectively. The oldest and largest child died at four months of gastroenteritis but the other 2 were living and well at the time the report was made. There were 3 separate placentas and fetal sacs.

The case which I wish to report is similar to those previously reported, in that the correct diagnosis was not made without the aid of the roentgenologist. That this aid in diagnosis is being used more frequently as time goes on is illustrated by the fact that 5 cases were reported before 1930 and 4 since that time. It seems reasonable to presume that, in the future, the presence of triplets will be recognized more often before delivery by the use of this valuable method of examination.

CASE REPORT

Mrs. M. T., white, aged twenty-three years, para 0-0-0-0 was first seen on Sept. 9, 1935, having been referred by her family physician for prenatal care and delivery. Her father died of "a fever and asthma" and her mother following "a stroke." The family history was otherwise negative. There was no history obtainable of multiple pregnancy in the family of either the patient or her husband. The patient's past history was negative except for tonsillectomy one year ago for hypertrophied tonsils.

Menses began at the age of fourteen years and were always regular every twenty-eight days, lasting three days with slight pain. The last period began May 5, 1935, making the estimated date of confinement Feb. 12, 1936. She had had some nausea and vomiting associated with slight headaches early in her pregnancy. There had been no edema or bleeding. Her bowels were regular, but she complained of hemorrhoids which gave her some discomfort at times. Fetal movements had not been felt. She stated that her general health was excellent and that she felt well.

Examination: Head and neck were negative, lungs clear, heart sounds normal. Breasts were well developed and contained colostrum. The abdomen was negative except for the enlarged uterus which seemed larger than the period of gestation would indicate. Height of the fundus uteri from the symphysis pubis was 18 cm. and estimated duration of pregnancy was twenty-four to twenty-six weeks. The position of the fetus could not be determined and the fetal heart could not be heard. Pelvic measurements were within normal limits, blood pressure 110/70, weight 107 pounds. Patient said her usual weight was around 90 pounds. Urinalysis showed nothing abnormal. On October 18 the blood pressure was 120/80, weight 116½ pounds, height of the fundus uteri 23 cm. It was still impossible to determine the position of the fetus and the fetal heart could not be heard although the patient said she felt movements. Moderate hydramnios was noted at this time, but in spite of the abnormal tension of the uterus and the rather rapid distention of the abdomen, the patient said that she felt well and was able to walk long distances without tiring. On November 1 the height of the fundus had increased to 28 cm., the circumference of the abdomen at the level of the umbilicus was 89 cm., and there was more tenseness from the increased hydramnios. Her weight at this time was 120½ pounds. Because the hydramnios had increased so markedly, and it was still not possible to palpate the fetus, a roentgen examination was decided upon to determine, if possible, the presence of twins or a monstrosity. At this time a ballottable mass could be felt just above the symphysis and a fetal heart could be heard about the level of the umbilicus and 3 cm. from the midline

on the left. The roentgenologist reported on November 4 that the examination revealed the presence of triplets, the first fetus presenting by the occiput with the back to the right, the second as a transverse presentation with the head to the left, and the third as a breech presentation with the back to the left.

An attempt was made to control the hydramnios by limiting the fluid intake, and a careful fluid record was kept until the date of delivery. At no time was there more than a normal variation between the fluids taken in and those excreted. Whether the hydramnios decreased or not is open to question. However, it can almost be said with certainty that it did not increase. During the five and one-half weeks between the time of diagnosis of multiple pregnancy and delivery, fetal parts gradually became palpable but at no time was it possible to outline a single fetus

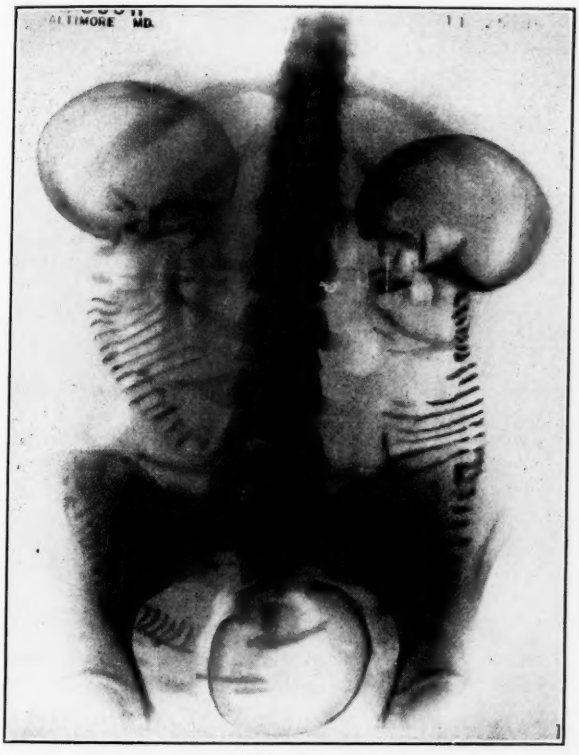

Fig. 1.

nor could more than one fetal heart sound be heard. A second x-ray taken two weeks after the first one revealed 2 fetal heads in the fundus and 1 in the pelvis (Fig. 1). The gain in weight continued, and on December 9, the patient weighed 129½ pounds. The height of the fundus was 30 cm., the distance from the symphysis to the top of the fundus around the ovoid was 38½ cm., and the circumference at the level of the umbilicus was 91 cm. During this time the patient felt well and had no complaints except some shortness of breath on exertion. The blood pressure remained around 120/80, urinalysis was negative, and hemoglobin was 80 per cent (Dare).

On December 10, at approximately thirty-one weeks of gestation, at 2:30 A.M., the foremost bag of waters ruptured spontaneously and labor pains began about one hour later. Labor progressed rapidly and normally. Pains were at three-minute

intervals, strong and lasting forty to fifty seconds. At 6 A.M. the cervix was completely dilated and the occiput of the first baby was on the perineum. Under gas-oxygen-ether anesthesia a left mediolateral episiotomy was done and low forceps applied. A 2 pound 13¾ ounce living female child was delivered at 6:05 A.M., position R.O.A. The second bag of waters presented and was ruptured artificially. This child presented as a footling breech with the back to the right. At 6:09 A.M. a 2 pound 13½ ounce living female child was extracted. After the delivery of the second child, the third one which had been a breech presentation with the back to the left turned spontaneously and presented by the occiput with the back to the right. The third set of membranes were ruptured and a combined podalic version followed by breech extraction was done. This child, also a female, was delivered at 6:17 A.M. and weighed 2 pounds 11½ ounces. The episiotomy was repaired with No. 2 chromic catgut, and the placenta and membranes were expressed intact by modified Credé method. There was very little blood loss but the patient's pulse rose to 120 per minute immediately following delivery and remained at that level for about half an hour, after which time it fell slowly to 80 per minute and remained at that level. The rise was attributed to the sudden decrease in intraabdominal pressure. The amount of amniotic fluid contained in each of the 2 sacs artificially ruptured was estimated at 1,000 to 1,500 c.c. The mother left the delivery room in

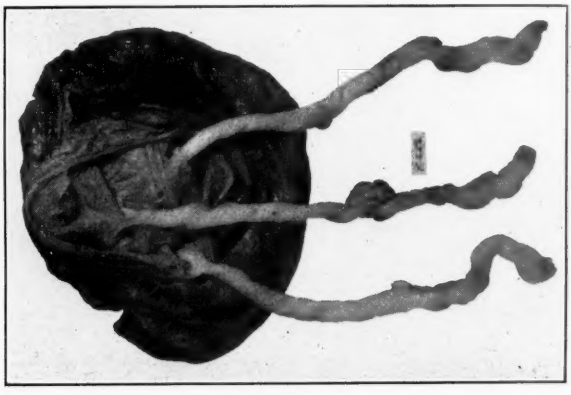

Fig. 2.

good condition. The puerperium was normal except for a rise in temperature to 100.8° F. on the fourth day and 101° on the fifth day, the pulse rate being 102 and 90, respectively.

All of the babies were normal but were very cyanotic and required resuscitation. After an hour in warm tubs and the administration of oxygen carbon dioxide they were breathing regularly, and their color was good although they cried poorly. They were then placed in premature cribs and taken to the premature room. Attacks of cyanosis recurred during the next few hours and six hours after delivery baby No. 2 died. A few minutes later baby No. 3 died during a cyanotic attack. Baby No. 1 died at the end of twelve hours in the same manner. The cause of death in all 3 was attributed to congenital atelectasis due to prematurity.

The placenta (Fig. 2) was large, round, and measured 18½ by 18 by 5 cm. The surface area was about that of the average placenta but the thickness was twice as great. It weighed 990 gm. or 490 gm. more than the weight of the normal placenta as given by DeLee.[10] Both the maternal and fetal surfaces were normal in color, and there was no evidence of any gross pathology. There were 3 amniotic sacs but only one chorion. All of the amniotic sacs seemed to be approximately the same size and were easily demonstrated as the ruptures were small and some

distance from the placenta. The membranes were entirely normal. The cords were large and all about the same length, 29, 30, and 31 cm. One cord had a velamentous insertion and 2 had central insertions. The placenta indicates that the case is one of uniovular triplets.

I wish to express my appreciation to Dr. Louis H. Douglass for his assistance in the handling of this case and in the preparation of this paper.

REFERENCES

(1) *Marcus, H.:* Gynéc. et Obstét., Paris **17:** 312, 1928. (2) *Edling:* Fortschr. a. d. Geb. d. Röntgen. **17:** 345, 1911. (3) *Essen-Möller:* Gynéc. et Obstét., Paris **2:** 146, 1920. (4) *Favreau and Despons:* Bull. Soc. d'obst. et de gynéc. de Paris **13:** 599, 1924. (5) *Genell:* Gynéc. et Obstét. **13:** 41, 1926. (6) *Johnston, Robert A.* (incorrectly reported as Johnson, Robert T.): Texas State J. Med. **20:** 570, 1925. (7) *Rowden, L. A.:* Brit. J. Radiol. **3:** 429, 1930. (8) *Trillat, Eparvier and Naussac:* Bull. Soc. d'obst. et de gynéc. de Paris **19:** 266, 1930. (9) *Aldridge, Albert H.:* Am. J. Obst. & Gynec. **24:** 140, 1932. (10) *DeLee, Joseph B.:* Principles and Practices of Obstetrics, ed. 4, p. 45.

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EARLY CHORIONEPITHELIOMA ARISING IN HYDATIDIFORM MOLE*

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THE diagnosis of chorionepithelioma is facilitated by the Friedman test due to the fact that the concentration of anterior pituitary hormone in the patient's urine is much higher than in the urine of a normal pregnancy. One-seventieth of a cubic centimeter of urine from a patient afflicted with chorionepithelioma may be sufficient to evoke a positive reaction in mice.[1] However, after the expulsion of a hydatidiform mole and curettage of the uterus, there may be a long latent period before the development of the chorionepithelioma, as in the case of Kroesing, which had a latent period of five and one-half years.[2] In the absence of clinical signs, such as bleeding, cystic degeneration of the ovaries, or irregular enlargement of the uterus, it is difficult to know whether a malignant tumor will eventually develop in a uterus from which a hydatidiform mole has been removed. In the case reported herewith a repeatedly positive Friedman test was the only indication of persistent intact mole tissue or early chorionepithelioma of the uterus.

L. K., white, aged thirty-one, para ii, was admitted to the hospital on April 24, 1934, with a history of profuse vaginal bleeding of twenty-four hours' duration with passing of blood clots. This had been preceded by irregular spotting since March 18. Her last regular menstrual period occurred Feb. 17, 1934. Upon a pelvic examination April 1, the diagnosis of a two months' pregnancy with threatened abortion was made. The patient stated at that time that in her previous pregnancies she also spotted during her second month.

Her past history was essentially negative. Her husband was living and well. She had had full-term deliveries six and four years previously. Her first pregnancy was complicated by a severe pyelitis and the delivery by a postpartum hemorrhage

*Read at a meeting of the Obstetrical and Gynecological Section of the Cleveland Academy of Medicine, June 6, 1936.

necessitating transfusion. Her second pregnancy was normal, but the delivery was followed again by severe postpartum hemorrhage. No transfusion was done. The child was stillborn (congenital heart disease). Her menses had always been regular, of average duration and flow. Physical examination, serology, and urinalysis were negative.

On admission to the hospital a diagnosis of incomplete abortion was made. No vaginal examination was done. Routine treatment with pituitary extract did not empty the uterus and did not check the bleeding.

Dilatation of the cervix and curettage was then performed on April 25, 1934. The uterus was found to be the size of that of a three months' pregnancy, its depth being 5 inches. A large mass of tissue grossly characteristic of hydatidiform mole was removed, and the uterus was gently curetted and packed.

Microscopic Examination: Uterine contents: Section showed a striking picture; the tissue was composed of chorionic villi, the majority of which showed moderate to marked edema of the stroma. Some of the villi were over 1½ mm. thick. The syncytium was thicker than average, nuclei of cells large. Final Diagnosis: hydatidiform mole (Fig. 1).

Fig. 1.

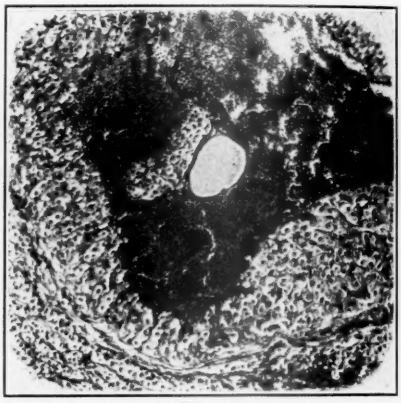

Fig. 2.

First. 1.—Photomicrograph, low magnification. Hydatidiform mole removed at first curettage.

Fig. 2.—Photomicrograph, low magnification. Rabbit ovary. Corpus luteum with hemorrhage and retained ovum (positive Friedman test).

The patient left the hospital in four days, at which time there was only a scant brownish vaginal discharge.

The admission specimen of urine (Apr. 24, 1934) gave a strongly positive Friedman test (Fig. 2), using ½ c.c. of urine (Table I).

A second Friedman test performed May 16, 1934, about three weeks after removal of the mole, gave a weakly positive result using 30 c.c. of urine. Because of the fact that gonadotropic hormone was still present in the urine, another Friedman test was done June 8, 1934, and again gave a weakly positive result with 30 c.c. of urine.

Because of the persistently positive Friedman reaction, it was thought advisable to repeat the curettement to remove whatever mole tissue might have been left in the uterus after the first curettement. The patient was readmitted on June 21, 1934. Examination on admission showed the uterus well involuted, not tender, no enlargement or tenderness of the adnexa. The history of a slight intermittent brownish discharge was the only finding pointing to a possible retention of hydatidiform mole in the uterus.

Dilatation and curettage was done on June 22, 1934. The uterus was found to be about 3 inches deep and was firm. The uterus was curetted carefully, but vigorously, with a sharp curet. Only a small amount of endometrial tissue was obtained.

Microscopic examination of the curettings showed a few small islands of uterine endometrium with glands few in number. There was some proliferation of fibroblasts and focal areas of round cell infiltration in the stroma. No villi or hydatidiform mole were present. Diagnosis: subacute endometritis (slight).

TABLE I

DATE	FRIEDMAN TEST		SURGICAL PATH. DIAGNOSIS
	RESULT	AMT. URINE	
4/24/34	Strongly positive	0.5 c.c.	Hydatidiform mole
5/16/34	Weakly positive	30.0 c.c.	
6/ 8/34	Weakly positive	30.0 c.c.	
6/22/34			Chronic endometritis
7/20/34	Strongly positive	30.0 c.c.	
7/30/34	Strongly positive	20.0 c.c.	
8/ 4/34	Strongly positive	30.0 c.c.	
	Negative	0.5 c.c.	
8/13/34			Few intact villi of hydatidiform mole
8/25/34	Weakly positive	30.0 c.c.	
9/14/34	Weakly positive	30.0 c.c.	
9/18/34	Positive	30.0 c.c.	
9/24/34			Intact syncytial masses of mole in uterus. Beginning chorionepithelioma (?)
9/26/34 Postop.	Negative	30.0 c.c.	
10/ 6/34 Postop.	Negative	30.0 c.c.	
10/31/34 Postop.	Negative	30.0 c.c.	
10/10/35 Postop.	Negative	30.0 c.c.	

The Friedman test was repeated one month after her discharge from the hospital (July 20, 1934) using 30 c.c. of urine, and a strongly positive reaction was obtained. Ten days later (July 30) her urine again gave a strongly positive Friedman test with 20 c.c. of urine. This was rechecked August 4, and the result was as follows: Friedman test strongly positive with 30 c.c. and negative with ½ c.c. of the patient's urine.

The patient was readmitted to the hospital August 12 solely because Friedman tests were persistently positive. The history and physical findings on this admission were entirely negative. There had been no vaginal bleeding or discharge since the last curettage seven weeks previously.

Curettage was again performed on August 13. The uterus was found to be about 3 inches deep and firm; no masses or irregularities were discovered on palpation. At one point in the curettage of the posterior wall profuse bleeding occurred. A small amount of endometrium was removed. The largest mass was about 6 mm. in diameter and appeared membranous, spongy and edematous. Microscopic examination of the curettings showed about a dozen typical chorionic villi of hydatidiform mole. The edema of the stroma was variable. In places some of the villi were over 1 mm. in width. The syncytium varied in thickness; in places it was heaped up with some of the nuclei, large and hyperchromatic. There was one small nest of cells several hundred micra in diameter, possibly decidual cells. Final Diagnosis: intact chorionic villi of hydatidiform mole.

Following this curettement a Friedman test was done Aug. 25, 1934, and was weakly positive with 30 c.c. of urine. On repeating the test about three weeks later, September 14, a similar reaction was obtained. However, a few days later, September 18, on repeating the test a somewhat more strongly positive result was obtained.

A pelvic examination on September 20 showed cystic enlargement of both ovaries to about three times the normal size. This finding, together with the fact that at no time was a negative Friedman test obtained with 30 c.c. of the patient's urine during the six-month period of observation, indicated increased hormonic activity resulting from the presence of living chorionic tissue in the uterus, and hysterectomy was decided upon.

The patient was readmitted to the hospital for the fourth time on September 23. She had no complaint. There was no vaginal discharge. The uterus was normal size, freely movable, not tender. The left ovary was cystic and four times the normal size. The right ovary was cystic and twice the normal size.

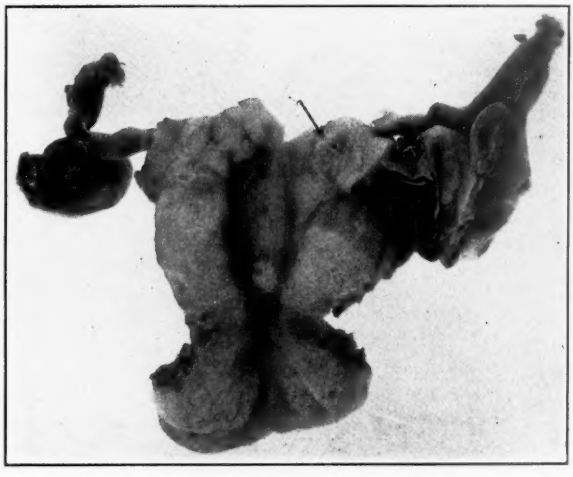

Fig. 3.—Gross photograph, actual size. Ovaries, fallopian tubes, uterus and cervix, showing necrotic mole mass in fundus and multiple cystic corpora lutea in ovaries.

On September 24 the following operations were performed: total hysterectomy, bilateral salpingectomy, left oophorectomy, and partial resection of the right ovary.

Laboratory Report: The uterus was of approximately average size (weighing together with the cervix about 65 gm.) and showed no appreciable abnormalities on the external surface. On opening the uterus the endometrial canal was not enlarged and the endometrium was thinner than average with no evidence of retained hydatidiform mole. On section of the myometrium, however, a striking picture presented in the upper portion of the fundus. Here a roughly spherical mass, about 12 mm. in diameter, was found reaching from just beyond the endometrium to within 1 mm. of the perimetrium (Fig. 3). The tissue here was friable in consistence and grayish yellow, grossly suggesting malignant tumor invading the myometrium. Microscopic examination of this area showed the tissue to be degenerating and necrotic tissue of hydatidiform mole (Figs. 4 and 5) and apparently not the tissue responsible for the positive Friedman tests. Further examination of the uterus to determine the cause of the most recent positive Friedman tests showed in the myometrium bilaterally toward the cornua small coherent masses of

grayish tissue in the walls of dilated and tortuous veins (Figs. 6, 7, 8, and 9). Sections from these areas showed very large syncytial cells or cell masses, some over 100 micra in diameter, adjoining one another in one or several layers immediately below the intima. The nuclei were very large, many hyperchromatic. In a few places coherent nests of these large cells were observed; the largest, about 1½ by ¾ mm., suggested beginning or early chorionepithelioma formation. The majority of the cells here were apparently intact.

Fig. 4.

Fig. 5.

Fig. 4.—Photomicrograph, very low magnification (about × 6). Degenerating and necrotic tissue of hydatidiform mole in myometrium of fundus.

Fig. 5.—Photomicrograph, low magnification. Degenerating and necrotic tissue of hydatidiform mole from area shown in Fig. 4.

Fig. 6.—Photomicrograph, very low magnification. Intact syncytial cells and cell masses lining veins in myometrium in cornua of uterus.

The fallopian tubes grossly appeared normal, but in the proximal end of the left tube there was a mass of friable whitish tissue in the wall several millimeters in diameter. Sections in this area showed, in the wall several hundred micra from the lumen, a mass 2 to 3 mm. in diameter, composed of necrotic mole tissue (Fig. 10).

The left ovary and the removed portion of the right ovary were both found to be enlarged by characteristic cystic corpora lutea (Fig. 3). There were two of these in the left and one in the right ovary, each measuring about 3 cm. in diameter. Microscopically, regional to a lutein cyst there was an island of typical decidual

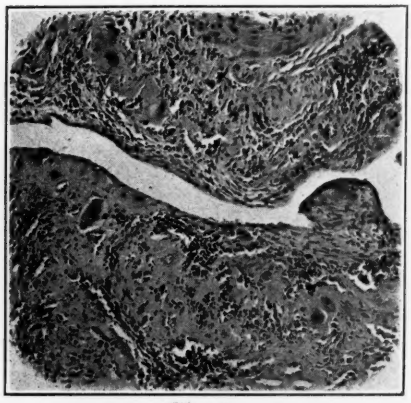

Fig. 7.

Fig. 8.

Figs. 7 and 8.—Photomicrographs, low magnification. Intact and degenerating syncytial cells lining veins in myometrium in cornua of uterus.

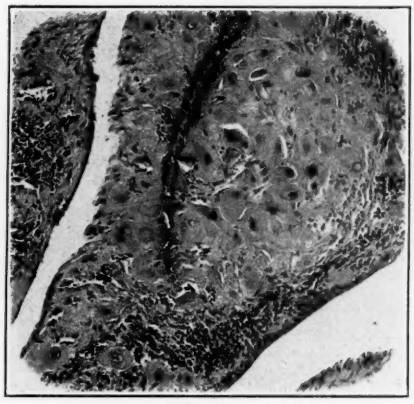

Fig. 9.

Fig. 10.

Fig. 9.—Photomicrograph, low magnification. Intact syncytial cells and cell masses with very large hyperchromatic nuclei lining veins, suggesting early chorionepithelioma formation.

Fig. 10.—Photomicrograph, very low magnification. Proximal portion of fallopian tube showing necrotic mole tissue in the wall.

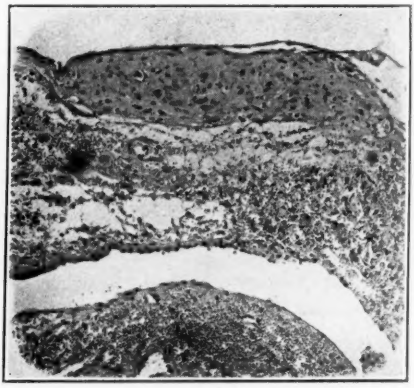

Fig. 11.—Photomicrograph, low magnification. Decidual reaction on surface of ovary (same magnification as Figs. 7 and 8) for comparison of size of nuclei of decidual cells and those of syncytium.

tissue several hundred micra in diameter just below the surface of the ovary (Fig. 11). There were also other smaller islands of similar decidual tissue at some distance just below the surface of the ovary.

Final Diagnosis: Multiple islands of intact syncytial cells in the walls of veins in the myometrium especially in the region of the left cornua. One island 1½ mm. diameter (beginning or early chorionepithelioma?). Disseminated intact hydatid mole masses in veins of uterus especially at left cornua and right lateral portion of fundus. Multiple areas of degenerating syncytial cells with replacement fibrosis in the walls of veins. Extension of hydatidiform mole into myometrium of fundus in an area 1½ cm. diameter reaching to within 1 mm. of the perimetrium (degenerated). One mole mass in wall of proximal portion, left fallopian tube (degenerated). Multiple cystic corpora lutea, ovaries largest about 3 cm. diameter.

The Friedman test on Sept. 26, 1934 (forty-eight hours after operation) was negative. The patient made a most uneventful recovery and left the hospital twelve days after operation. The Friedman test on the day of discharge was negative. It was also negative Oct. 31, 1934, and Oct. 10, 1935. At the time of the present report (Nov. 1, 1935), the patient has no complaint and the pelvic findings are entirely negative.

COMMENT

The incidence of chorionepithelioma following hydatidiform mole has not been definitely established. Findlay reports a series of 500 cases of hydatid mole. In 157 of these, chorionepithelioma developed, an incidence of 31.4 per cent.[3] In Senarden's series of 49 moles, 5 or 13 per cent developed chorinepithelioma; while Williams states that in his experience only 5 per cent of hydatidiform moles underwent chorionepithelioma[4] formation.

Because of such variation in the incidence of chorionepithelioma developing in hydatidiform moles recorded by different observers, the method of treatment is often debatable. One of the authors (M. G.) has sent the complete history of this case to twelve outstanding obstetricians and gynecologists of his city asking their opinion as to what treatment was indicated. Fifty per cent of the responses were in favor of immediate hysterectomy, while the rest advised watchful waiting.

During the six months that elapsed from the discovery of the mole to the hysterectomy, the Friedman test remained positive with 30 c.c. of the patient's urine, and repeated pelvic findings were negative. As soon as the Friedman test appeared more positive and the ovaries showed a cystic enlargement, the operation was performed without delay.

It appears, then, that repeated examination of the patient's pelvis, together with repeated Friedman tests, may be used as a reliable guide in solving the often perplexing problems of the treatment of hydatidiform mole.

REFERENCES

(1) *Schumann, E. A.:* Curtis, Obstetrics and Gynecology 2: Philadelphia, 1933, W. B. Saunders Co., p. 962. (2) *Kroesing, E.:* Arch. f. Gynäk. 88: 469, 1909. (3) *Findlay, P.:* Am. J. Obst. 75: 15, 1917. (4) *Schumann, E. A.:* Am. J. Obst. & Gynec. 4: 586, 1922.

Enea, Domenico: Chemical Surgery of the Pelvic Sympathetic in Essential Vulvar Pruritus, Clin. ostet. **9:** 549, 1935.

The author reports a case of pruritus vulvae cured by phenolization of the pelvic sympathetic nerve after having resisted all other known treatments for fifteen years.

AUGUST F. DARO.

STUDIES ON BARBITURATES. XIV

The Placental Transmission of Nonanesthetic Doses of Barbital

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Anesthetic doses of barbital and amytal have been shown to pass from the blood of the mother into the fetus.[1] In these experiments single anesthetic doses of sodium barbital (from 225 to 300 mg. per kg.), and amytal (100 mg. per kg.) were administered intravenously to pregnant rabbits, and the amounts of barbiturate present in the fetus, amniotic fluid, and placenta were determined by colorimetric methods for the quantitative estimation of barbiturates developed by Koppanyi et al.[2, 3] It was found that appreciable quantities of these two barbiturates were present in the fetus fifteen minutes after the administration of the drug to the mother, and in some cases the quantity approached a concentration which could be deemed anesthetic. However, in all cases the fetuses were viable as shown by their response to mechanical stimuli. Since the doses used in this work were higher than those used in human obstetrics, the possibility arises that in smaller doses barbiturates are not transmitted through the placenta in detectable amounts. The following experiments were devised to investigate this possibility.

EXPERIMENTAL

Sodium barbital (soluble barbital, "medinal") in doses of 75 and 100 mg. per kg. was administered to rabbits by the marginal ear vein. These amounts are sedative and soporific for rabbits, but never produce true anesthesia. This drug was chosen for this work in preference to other barbiturates, because a fairly large amount of it may be given without obtaining profound depression of the central nervous system, and thus it is easier to estimate accurately the amounts of drug present in the tissues without administering anesthetic doses.

In previous experiments when barbiturates were used in anesthetic doses, the surgical procedures involved could be easily carried out. In this series of experiments, however, since nonanesthetic doses were administered, the surgical procedures could not be performed without further anesthesia. Therefore, for immobilization and analgesia of the experimental animal, spinal anesthesia was used in every case. One cubic centimeter of a "light" type of spinal anesthetic (novocaine 0.195 gm., starch 0.130 gm., alcohol 0.324 c.c., and physiologic saline q.s. ad 2.000 c.c.) was injected into the third lumbar interspace and after the maximum effect was obtained the rabbit was placed on an animal board, head downward, and the requisite dose of sodium barbital injected. After laparotomy and exposure of the uterus two or more fetuses were removed at various intervals by clamping off and excising the portion of the uterus containing the fetus. Care was taken not to interfere with the circulation of the remaining portion of the uterus, which was returned

to the abdominal cavity and the wound temporarily closed until the removal of the next uterine portion. The excised portion of the uterus was opened longitudinally, and the amniotic fluid was collected without contamination with blood by aspirating it from the amniotic sac with a syringe. The fetus was separated from the placenta and fetal membranes, and tested for viability by pinching a fold of the skin with forceps.

The fetuses, the placentas, and amniotic fluids were prepared for barbital determinations separately. The fetuses were weighed, hashed in a meat grinder and the proteins precipitated and removed by filtration according to the alkaline-copper sulphate method described by Koppanyi et al.[2, 3] The placentas were treated likewise. The amniotic fluid was measured and treated with equal amounts of 10 per cent sodium tungstate and 5 per cent sulphuric acid, shaken vigorously to precipitate the proteins and filtered. The protein-free filtrates were then extracted with chloroform. All chloroform extracts of the filtrates were concentrated by evaporation and tested by the microtest of Koppanyi et al.[3]

TABLE I. THE CONCENTRATION OF BARBITAL IN THE AMNIOTIC FLUID, PLACENTA AND FETUS FOLLOWING INTRAVENOUS ADMINISTRATION OF SODIUM BARBITAL TO THE MOTHER

RABBIT	DOSE MG./KG.	TIME ELAPSED BETWEEN INJECTION AND REMOVAL OF THE FETUS	AMNIOTIC FLUID MG./C.C.	PLACENTA MG./GM.	FETUS MG./GM.
1	75	1 min.	trace	trace	trace
		15 min.	0.040	0.015	0.008
		30 min.	0.025	0.023	0.010
		60 min.	0.025	0.024	0.010
2	100	1 min.	----	0.029	0.017
		15 min.	----	0.023	0.014
		30 min.	0.013	0.015	0.027
		60 min.	----	0.048	0.048
3	100	5 min.	0.010	0.010	0.008
		30 min.	0.017	0.025	0.022

Table I contains a summary of the results obtained using doses of 75 and 100 mg. of sodium barbital per kilogram. With these doses, as with the larger doses used in previous work, a transfer of barbital from the mother to the fetus could easily be demonstrated. Barbital was found in the placenta and in the amniotic fluid as well as in the fetus. The amount of barbital accumulation in the placenta and fetus increased steadily within the first hour following intravenous injection. To approximate conditions existing in normal obstetric use, only pregnant rabbits which were near the end of gestation, when the weight of the fetuses was about 15 to 20 gm., were selected for these experiments.

COMMENT

The doses of barbital administered to these pregnant rabbits represent less than one-half of the minimum amount of this drug required to produce surgical anesthesia. Corresponding doses of other barbiturates are frequently employed in obstetrics to produce amnesia and analgesia, and from these experiments, it is evident that doses of this magnitude permeate the placenta just as easily as anesthetic doses. In our previous work it was shown that the placenta presents no barrier against full anesthetic doses of barbituric acid derivatives,

and this is also true for doses producing only light depression. There is little doubt that what holds true for these smaller doses of barbital also applies to corresponding doses of other barbiturates. At any rate, no one can now maintain that the placental permeability to barbiturates exists only after large doses have been administered.

In the experiments described above, all of the fetuses removed from the uterus showed respiratory movements and reacted to mechanical stimuli. They were not anesthetized, in fact they could not be, for no anesthetic doses had been administered to the mother. But the fact that fetal tissues contained appreciable amounts of barbiturates is a fairly certain indication that some degree of central nervous depression must have been present in the fetuses, and that the degree of this narcosis of the fetus will depend upon the size of the dose administered to the mother. While we are not prepared to state that pregnancy offers a contraindication to the use of barbiturates, we must call attention to the fact that the placenta offers no barrier to barbiturates, and that whenever these drugs are administered to expectant mothers, the embryo will get its full share of them.

REFERENCES

(1) *Dille, J. M.:* J. Pharmacol. & Exper. Therap. **52:** 129, 1934. (2) *Koppanyi, T., Murphy, W. S., and Krop, S.:* Arch. internat. de pharmacodyn. et de thérapie **46:** 76, 1933. (3) *Koppanyi, T., Dille, J. M., Murphy, W. S., and Krop, S.:* J. Am. Pharm. Assn. **23:** 1074, 1934.

ERGOT IN THE PUERPERIUM

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(From the Kensington Hospital for Women)

THE clinical value of ergot in the puerperium has long been questioned by various obstetricians. However, Koff[1] and Moir[2] have definitely proved that ergot has a marked oxytocic effect and an important place in the puerperal management of a modern obstetric case. In view of the divergent opinions on the importance of ergot, we have studied the morbidity, involution, and puerperal bleeding in 551 postpartum cases on three different ergot regimes in the Kensington Hospital for Women.

PROCEDURE

In each case every patient received an ampule of pituitary solution and ergot at the completion of the second stage of labor. The first 100 patients received no other oxytocic medication during their stay in the hospital. A series of 351 patients received fluid extract of ergot, U.S.P., starting when the patient was taken to her ward bed. Here she received one drachm every four hours for six doses, and then three times a day for four days. In the third group of the series, 100 cases, an ergot preparation* was used which was standardized for its content of the new

*Ergoklonin, supplied through the courtesy of John Wyeth and Brother, Inc.

alkaloid, ergostetrine[3] (ergometrine). This was administered in the same way as the fluid extract. In those cases where lochia rubra was present to any great extent after the sixth postpartum day an additional course of one drachm at four-hour intervals for six doses was administered. Thirty-five per cent of the patients on fluid extract of ergot, U.S.P., needed this and 20 per cent on ergoklonin received additional dosage. Upon discharge date, the morning of the tenth day, a sterile vaginal examination was done on all patients that did not have repair work following delivery. At this time note was made of the involution of the uterus, the amount of bleeding, and the gross uncorrected morbidity.

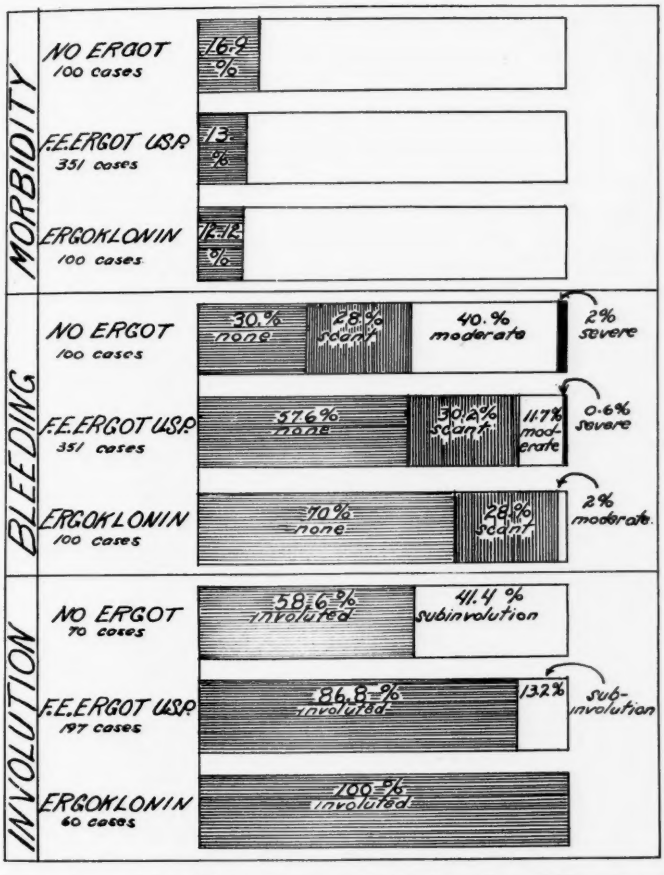

Fig. 1.—Comparison of involution, degree of bleeding and morbidity in patients on different regimes during the puerperium.

RESULTS

Involution.—In patients not receiving ergot, subinvolution occurred in 41.4 per cent of the patients examined (Fig. 1) and in 13.2 per cent of the patients of the fluid extract series, while no subinvolution occurred in the patients receiving the newer ergot preparation.

Bleeding.—A striking difference in the lochia rubra was noted on the tenth day (Fig. 1). The best result was obtained with ergoklonin, since 70 per cent of that group had no sanguineous discharge. The fluid ex-

tract series showed bleeding to some extent in all but 57.6 per cent, while in the cases without oral ergot only 30 per cent were entirely free of bleeding. In the patients classified as showing scant bleeding (Table I), there was a low incidence of subinvolution, and these may therefore be

TABLE I

DEGREE OF BLEEDING	NO ERGOT				F. E. ERGOT U.S.P.				ERGOKLONIN			
		100 CASES				351 CASES				100 CASES		
	PER CENT	INVOLUTED	SUBINVOLUTION	NO EXAMINATION	PER CENT	INVOLUTED	SUBINVOLUTION	NO EXAMINATION	PER CENT	INVOLUTED	SUBINVOLUTION	NO EXAMINATION
None	30	21	2	7	57.6	117	3	82	70	40	0	30
Scant*	28	16	4	8	30.2	44	11	51	28	18	0	10
Moderate	40	4	22	14	11.7	10	11	20	2	2	0	0
Severe	2	0	1	1	0.6	0	1	1	0	0	0	0

*Scant bleeding: a few drops of fresh blood or a mucosanguineous discharge.
Moderate bleeding: a saturated vulval pad in six hours.
Severe bleeding: several saturated pads in six hours.

grouped with the nonbleeding series from the standpoint of a satisfactory puerperium. The groups showing moderate bleeding demonstrate clearly the value of oxytocic medication during the puerperium, for 40 per cent of the nonergot cases fall in this classification, while only 11.7 per cent in the fluid extract series, and 2 per cent in the ergoklonin series showed hemorrhage of this magnitude. The "severe bleeding" classification is represented by 2 per cent in the nonergot group and 0.6 per cent in the fluid extract cases. No cases of this type occurred in the ergoklonin group.

Morbidity.—A patient was considered as morbid when her temperature reached 100° F. twice in twenty-four hours, excluding the first postpartum day. These figures are uncorrected and constitute all temperatures, no matter what cause, that appeared in these 551 cases. The morbidity was highest (16.9 per cent) (Fig. 1) in the patients who received no ergot and lowest (12.12 per cent) where ergoklonin was used, while the fluid extract of ergot, U.S.P. series differed only slightly from the new preparation, at 13 per cent.

CONCLUSIONS

1. Lochia rubra was more persistent in patients receiving no form of ergot during the puerperium.

2. Subinvolution occurred in much higher percentage (41.4 per cent) in nonergot cases than in fluid extract cases (13.2 per cent), and was completely absent in the ergoklonin series.

3. A satisfactory puerperium was observed in 58 per cent of patients receiving no oxytocic drug, in 87.8 per cent of patients receiving fluid

extract of ergot, U.S.P., and in 98 per cent of patients treated with ergoklonin. There was less striking difference in the morbidity percentages in the three groups than in the figures showing degree of bleeding and subinvolution.

4. From a study of a series of 551 cases, ergot appears to be a useful and necessary aid to a normal puerperium, preferably in the form of a preparation of known ergostetrine (ergometrine) content.

REFERENCES

(1) *Koff, A. K.:* Surg. Gynec. Obst. **60**: 190, 1935. (2) *Moir, C.:* Brit. M. J. p. 1119, 1932. (3) *Thompson, M. R.:* J. Am. Pharm. A. **24**: 748, 1935.

RECOGNITION AND PREVENTION OF BLADDER INJURIES

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ON FIRST thought, a discussion of the subject indicated in the title of this paper would appear superfluous and exceedingly elementary. However, when one reads the literature and finds that the mortality in bladder injuries during operation is variously reported as from 12 to 45 per cent, it is apparent that the subject, after all, does deserve attention, especially as most cases remain unreported.

My own attention was drawn to this subject by a few observed and below described personal cases. My experience leads me to conclude that this injury is not a serious complication, provided that it is recognized and promptly and properly treated. Once the accident is recognized, surgical victory is almost surely attained, for treatment is simple and practically always successful.

This subject is of particular interest to the pelvic surgeon who of necessity employs the suprapubic incision in the great majority of cases, and as a corollary the bladder is in much greater danger than in other types of surgery except that of hernia. It is especially in jeopardy in cases of large fibroids of the uterus where the bladder is displaced and stretched and is likely to be found at a much higher level than normally. Practically all of my observed and personal cases of bladder injury occurred in large fibroids of the uterus.

CASE 1.—Mrs. L. M., forty-seven years old, gravida vii, para iii. Chief complaints: enlargement of the abdomen, dribbling of urine, and profuse menstrual flow.

Abdominal examination showed a mass in the center of the abdomen, hard, not tender, reaching from the symphysis to the umbilicus. Vaginal examination disclosed a marked cystocele, lacerated cervix, uterus the seat of tumors reaching to the umbilicus.

At operation, there was found a degenerated cystic mass which was firmly adherent to the parietal peritoneum and intestines and attached to the fundus of the uterus by a short pedicle. The tubes and ovaries appeared normal. The liver

was smooth and the gallbladder was normal. A median suprapubic incision was made, and a large amount of serous fluid escaped from the peritoneal cavity. The tumor was separated from the intestines and parietal peritoneum. One of the cystic masses opened during manipulation. The pedicle of the tumor was clamped, and the tumor was removed. A supravaginal hysterectomy was then performed, all raw surfaces were peritonized, and the abdomen was closed in layers, without drainage.

A culture from the intraabdominal fluid found free in the peritoneal cavity was found sterile.

The uterus contained many small intramural fibroids and measured 6 by 6 inches. The wall was very thick and the mucosa hypertrophic. The intramural fibroids appeared somewhat degenerated. Another mass distinct from the uterus was globular in shape and measured 9 by 8 inches. It included two large multilocular cysts with serous, yellow, gelatinous contents. The cyst wall was very thin, smooth and did not contain any papillae. The solid portion of the mass was yellowish in color, fatty and was also somewhat cystic.

Diagnosis: Cellular myomas of the uterus, pedunculated myoma with cystic degeneration, and marked endometrial hyperplasia.

Sections from various portions of the uterus and from the pedunculated mass showed extremely cellular leiomyomatous tumors which did not appear aggressive enough to warrant diagnosis of malignant transformation.

Postoperative Course: Patient was comfortable the day of the operation. She was catheterized twelve hours afterward and no urine was obtained. An intravenous infusion of glucose and saline was given, and she was again catheterized and only a few drops obtained. The nurse reported that the patient was almost continuously dribbling. A later catheterization yielded 25 c.c. of urine. The bladder was filled with argyrol solution and practically the same amount was obtained by catheterization as was introduced. The chemical examination of the blood showed a nonprotein nitrogen of 35, and a CO_2 of 40. Hot fomentations were applied to the kidney regions and hypodermoclysis and intravenous infusions were continued. A urologist was called in consultation, and he was of the opinion that the ureters were not tied, that there was no injury to the urinary organs, and that the patient was suffering from reflex anuria. The patient died about seventy-two hours after the operation.

Autopsy Report: On opening the abdominal cavity the viscera were found covered by plastic exudate and slightly adherent to each other. Line of suture was intact. On inserting a probe into the bladder there was found a small collapsed opening in the roof of bladder which connected with the peritoneal cavity. The opening was found to be the only part of a large surgically produced defect in the roof of the bladder, most of which was closed by inclusion within the sutures closing the peritoneal cavity. It was impossible to discern within the peritoneal cavity any argyrol which had been introduced into the bladder or any indigo carmine which had been injected intravenously. The bladder was empty and the mucosa congested. The microscopic examination of the kidneys and pelvic lymph nodes showed them to be normal.

CASE 2.—Mrs. R. F., aged twenty-five years. In the course of an examination for a gastrointestinal upset, her family doctor discovered a large tumor of the uterus. In retrospect, the patient recalled being troubled with urinary frequency. An abdominal examination revealed a large ovoid mass reaching from the symphysis to the umbilicus.

Operation: Median suprapubic incision, the bladder was very high and attached to the uterus. The bladder was dissected off and in doing so a small piece of adherent bladder was opened into. The rent was immediately repaired by two layers of sutures. A cigaret drain was placed in the pelvic cavity behind the cervical stump, and a piece of Penrose tubing was placed over the cut area. A retention catheter was placed in the bladder.

The uterus measured 10 by 6 inches, and contained several hard fibroids. The patient made an uneventful recovery.

CASE 3.—Mrs. F. H., aged forty years. Chief complaints: lower abdominal pain, enlargement of the abdomen, and menorrhagia. Vaginal examination revealed the presence of a uterus reaching from the pelvic basin to the level of the umbilicus. Multiple tumors were palpable. The patient was catheterized on the operating table and the catheter was left in situ. A suprapubic incision was then made and a typical supravaginal hysterectomy was performed. The bladder was at a much higher level than normally and was cut into. No urine escaped but the fact that the structure was bladder, was confirmed by feeling the catheter. The bladder injury was treated exactly as in the case cited above. The patient made an uneventful recovery.

CASE 4.—Mrs. L. B., aged forty-two years. The signs and symptoms were similar to those in Case 3. This patient was also catheterized on the operating table, and the catheter was left in situ. A suprapubic incision was made and a supravaginal hysterectomy was performed. A small intraligamentous fibroid was also removed. Toward the latter part of the operation, the bladder was opened. Recognition of this accident would have been doubtful had it not been for the presence of the catheter in the bladder. The bladder rent was repaired as in the two cases cited above, and the patient made an uneventful recovery.

In order to avoid this, to say the least, embarrassing complication, I have lately been employing the following method to identify the bladder: The patient is catheterized and the bladder urine is allowed to escape. The catheter is left in situ, and by means of a glass connecting tip and rubber tubing the catheter is connected to a glass calibrated reservoir suspended from a movable column stand. This tube rests on the patient's thighs and lies under sterile drapes. There is an additional connecting glass tip in the tubing between the reservoir and the catheter. The reservoir is the usual "clysis" or intravenous bottle. I usually have it filled with 300 c.c. of 4 per cent boric acid solution, and a nurse releases the clamp on the tubing and allows the bladder to fill as soon as, or just before, I commence the abdominal incision. As soon as I have recognized the bladder, I open into the peritoneal cavity, and the nurse then allows the bladder fluid to drain off by disconnecting the glass connecting tube which lies outside the sterile drapes. Should it become necessary to refill the bladder, it is a very simple matter to again reconnect the connecting glass. The catheter is removed after completion of the operation.

Since I have been filling the bladder, I operate with much greater comfort. I feel that I am treading on much surer ground. The chances for inadvertently opening the bladder are very greatly diminished, and should this accident occur, it would be very easily recognized and repaired.

Leaving a catheter in situ, even without distending it, is a valuable aid in recognizing the bladder.

I am convinced that bladders are at times opened, and if the bladder is empty, the fact that the bladder has been opened frequently escapes recognition. Peritonitis results, and if autopsy is not performed, the cause of the peritonitis is ascribed to some other factor.

REFERENCES

(1) *Gibson, C. L.:* Med. Rec. **51:** 401, 1897. (2) *Eggenberger, H.:* Deutsche Ztschr. f. Chir. Leipsic, October, 1908. (3) *DeGorma, W. B.:* New York State J. Med. **13:** 571, 1913. (4) *Stevens, W. E.:* California & West. Med. **39:** 388, 1933. (5) *Bierhoff and Unger:* Am. J. Surg. **30:** 506, 1935. (6) *Héinick, P.:* Surg. Gynec. Obst. **22:** 492, 1916. (7) *Leff, M.:* AM. J. OBST. & GYNEC. **29:** 749, 1935.

1882 GRAND CONCOURSE

ENDOMETRIOSIS OF THE UMBILICUS

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UNDER the caption of heterotopic endometrial growths are included such structures or tissues which morphologically and in certain respects functionally resemble the uterine mucosa, although not necessarily coming in direct contact with the latter.

The theoretic origin of and the bizarre nomenclature ascribed to the specific neoplasm under discussion has been fully dealt with elsewhere. Cursory reference to the theoretical phases should therefore suffice when emphasizing more important points in the cases here reported.

Lauche,[1] assuming that under proper conditions coelomic cells are capable of transmutation into endometrium, probably has the advantage over advocates of other theories, because his reasoning rests firmly upon an embryologic foundation which is all inclusive, in that the wolffian body and müllerian ducts which are brought in for culpability as etiologic factors are developmentally of coelomic origin (Cullen[2]).

CASE REPORTS

CASE 1.—(Record No. 38359.) Mrs. M. C., aged forty-three years, white. Previously admitted November, 1926, and operated upon by Dr. George Gray Ward, including curettage, trachelorrhaphy, perineorrhaphy, rectopexy, myomectomy, oophorectomy, fixation of prolapsed ovary. The pathologic diagnosis was glandular hyperplasia of the endometrium, cervicitis, hemorrhagic ovarian cyst, normal appendix, myomata uteri. Patient was relieved of symptoms, and the wound healed by primary union. She was discharged on Nov. 24, 1926. Patient readmitted April 22, 1930. There was a lump in the umbilicus, which was first noticed in June, 1928. On examination a nodule which was tender, red, and hard, was found. On March 6, 1930, examination revealed an increase in size of the mass, which was now uncomfortable; it was inclined to bleed a little and was tender.

At the operation a neoplasm of the umbilicus, the size of a large acorn was observed; it was solid, tender, bluish in color, increasing in size, entirely free from surrounding tissue in the abdominal wall and free from any connection with the peritoneum. The mass was excised in its entirety when incising the abdominal wall.

Examination.—A firm node covered with stretched skin presenting a few purplish vesicular formations the size of a millet seed. A transsection revealed the nodular

mass composed of whitish tissue septa which included in the meshes small cystic formations. Larger structures of the same type were filled with brownish, blackish thick fluid similar to old blood. The surrounding fat tissue was well delimited from the tumor, which did not seem to encroach upon it.

Serial sections of the whole mass were made, and every fifth and tenth section was prepared for microscopic studies. The epidermis covering the mass varied in thickness and appeared normal. The nodular projections were produced by the inclusion of groups of glands, which were in most instances a dense dissemination of lymphocytes. Glands were of different sizes; their shape and the type of epithelium corresponded to endometrium; a secretory function was apparent in some of them. Where cystic distention had occurred, the epithelium was flat or of cuboidal type. The fibroepithelial structures were densely scattered in the periphery of the mass, while in the central portions the epithelial structures were almost missing and diffusely arranged strands of cytogenic tissue only were encountered.

There was no borderline between the corium and the fibroepithelium inclusions which were also found below the fascia. In this area the epithelium was generally of nonsecretory, moderately atrophic type. One of the glandular ducts was dilated to a small cystic formation which was occupied by small lobules of fatty tissue. Near to it was a strand of loosely arranged cytogenic stroma in which polynuclear giant cells were densely distributed.

Since the peritoneum was not demonstrable in any of the sections, a continuity of the endometrial structures with the peritoneum could not be made evident. There were no specific epithelial formations found in the lower part of the subfascial layer and in the muscle. There was no evidence of inflammation.

Diagnosis.—Adenoma of umbilicus of endometrial type (endometrioma of umbilicus).

CASE 2.—(Record No. 59718.) Mrs. S. G., aged thirty-three years, colored. She was admitted June 10, 1935. Operator: Dr. A. J. Murphy. Patient complained of soreness and bulging of navel for four years. Her menses recorded 12 × 28 × 6-9, occasional clotting, no dysmenorrhea, last regular period May 20. She had been married for thirteen years and was never pregnant. She was never operated upon. The umbilical swelling about the size of the "tip of finger" was getting progressively worse. She was not aware that coughing or exertion caused any increase in the size of the growth.

On operation a small umbilical hernia was found; there was no intestine or omentum in the hernial sac.

Clinical Diagnosis.—Umbilical hernia.

Gross Specimen.—Excised umbilicus with subcutaneous tissue. The umbilicus proper was converted into a dome-shaped elevation 2 cm. in diameter. The lower severed surface revealed a funnel-shaped indentation in which scar tissue was apparent. A transverse section through the specimen opened a cyst cavity which was partly filled with tarlike liquid. Its upper portion was composed of the projecting umbilicus. A smaller compartment laterally was lined with smooth serosa and released clear fluid. The tissue surrounding the cystic cavities was yellowish, firm connective tissue.

The endometrium presented a premenstrual phase. The myometrium was regularly built. Myomas changed from microscopic sizes to the large sizes described and revealed in all instances of typical structure. The serosa of the uterus was greatly thickened in areas and included minute cystic formations at such places, which were partly lined with flattened unspecific epithelium, in some instances of higher cuboidal type. There were multiple calcified deposits, many of them of the type of psammoma bodies. The section through the umbilicus revealed cystic cavities

lined with a folded, generally cuboidal epithelium arranged in a simple row. In one area short papillas were noted, the stroma of which included aggregated pseudoxanthoma cells. In a single spot a polyus structure was found built of the same structures as endometrium with a stroma infiltrated with round cells. Glands bore the characteristics of endometrial glands, however, did not show secretory function. Fragments of organized blood coagula were either adherent to the inner surface or lying free in the lumen. The subjacent stroma of the cyst wall which did not differ from the subcutaneous tissue was occupied in parts by hemorrhage of old age. Other cystic compartments described in gross examination bore the same epithelial lining, however, did not include structures identical with endometrium.

Diagnosis.—Adenofibrohyperplasia of umbilicus (endometriosis).

CASE 3.—(Record No. 60217.) Miss A. S., aged forty years, single, white, was admitted Aug. 28, 1935. Her chief complaint was bleeding from the umbilicus three to four days prior to each period for the last four or five years. Catamenia 13 × 28 × 2-5 without pain or clots; last menses August 1, likewise regular. She was not married and never pregnant. No previous operation. Except for umbilical symptomatology and occasional parietal and occipital headaches just prior to her periods and a feeling of pelvic pressure or heaviness, and a rapid gain in weight during the last four years, patient otherwise felt and looked well.

At operation a granular cervicitis and inclusion cyst of the vagina were found. There was no growth on, nor enlargement of the umbilicus which was normal in contour. Probing with a very fine wire did not detect any opening through which bleeding from deep structures might have occurred. There was nothing to indicate any peritoneal attachment or abdominal continuity of the umbilical scar with any intraabdominal structures, as incision was advanced down to the peritoneal cavity.

Pathologic Examination.—Clinical diagnosis: endometriosis of the umbilicus. The gross specimen showed an umbilicus which was continuous with a concentric tumorlike enlargement of the subcutaneous fat tissue and measuring about 1 cm. in diameter. Microscopically the tumor of the umbilicus was composed of glands lined with cuboidal and cylindrical epithelium which was similar to that found in the derivatives of the müllerian duct. The glands formed adenoma-like structures, producing lobules separated from each other by a more or less broad layer of fibrous tissue. The individual glands were surrounded in some instances by thin layers of cytogenic stroma, resembling the endometrial. The glands were very close to the squamous epithelium covering the external surface. Some of the glands were cystically dilated and lined with flattened low cuboidal epithelium. The stroma around the glands included greatly engorged, large, thick-walled blood vessels and massive aggregations of pseudoxanthoma cells.

Diagnosis.—Partly cystic endometroid adenofibroma of umbilicus (endometriosis).

No complaints referable to original umbilical pathology in any of these cases recorded in follow-up to date. In none of the three patients was there any connection of the umbilical structures with any peritoneal or intraabdominal tissues. Similar findings have been reported by Green,[3] Goddard,[4] Zitronblatt,[5] Keitler,[6] Schiffmann and Seyfert,[7] and Roques.[8] It is relatively infrequent that such heterologous pathologic tissue has no connection with the peritoneum.

The total of reported cases throughout the world at the end of 1935 is sixty-eight.[9-17]

It is noteworthy, that a predominance occurs in white individuals. No case has been reported from Africa, the Far East, or the Orient, yet the colored individuals are not immune as indicated by our Case 2, Record 59,718 and the reports of others.

COMMENT

Absence of tumor (visible or palpatory) must be evidence of an exfoliative or desquamative process in the umbilical tissue when the bleeding occurs. Such an outcome may probably be the end-result of a conditioning influence exerted by an estrogenic hormone, which as is known appears in the blood in greater concentration during the premenopausal and early menopausal periods. The dormant endometrial structures becoming activated by a more pronounced stimulus, then begin to function, as was probably the effect in Case 3, where for twenty-two years of the patient's twenty-seven active menstrual years, no bleeding had occurred.

The result indicated must be predicated upon the presence of endometrial tissue in the umbilicus, derived most likely from an embryologic coelomic residium or cell arrests, which, judging from the infrequency of such pathology (3 in 37,355) gynecologic cases reviewed in this study (the largest on record) occurs in an extremely circumscribed number of female ontogeny, in which the culpable cells, possessing potentiality for future differentiated biologic characteristics, begin to function for the first time under proper stimulation, probably hormonal (gonadotropic prolan A), or as the result of the removal of some antihormonal control.

The temptation to hypothesize in an endocrine sphere, in seeking a solution to some of the problems presenting themselves under the aforementioned caption, provokes the thought that at least some endocrine factor is responsible, particularly during the stage of gradual spontaneous castration (premenopause-menopause decade) due to a sort of reversed reciprocal relation between the ovaries and the gonad-stimulating cells of the anterior pituitary.[20]

It may readily be that the same explanation holds true for younger women in whom, as a result of a genital crisis, hyperfunctional reaction of the hypophysis occurs similarly, bringing about the same activation.

Witherspoon[21] has advanced a similar thesis and has attempted to prove by his pathologic material that the igniting factor of endometrioma has its origin in the excessive stimulation of the aberrant tissue, by the ovarian follicular hormone (prolan A). When this hormone's action is abnormal, there is produced a cellular metaplasia of the potential serosal cells or tumor proliferation of an aberrant endometrial implant, in short, the hormone is responsible for endometrial flowering.

Although operation offers a ready method for the relief of the symptoms associated with umbilical endometriosis, we must be mindful of other means at hand, to be used especially during the menopausal decade, in counteracting hormonal activation of endometrial tissue. Where the indications exist, the catalytic action of x-ray and radium may serve a well-defined purpose.

REFERENCES

(1) *Lauche:* Virchow's Arch. **253:** 298, 1923. (2) *Cullen:* The Umbilicus, Philadelphia, 1926. (3) *Green:* Trans. Path. Soc. London **1:** 243, 1899. (4) *Goddard:* Surg. Gynec. Obst. **9:** 249, 1909. (5) *Zitronblatt, D.:* Med. Wchnschr. **39:** 371, 1923. (6) *Keitler:* Monatschr. f. Geburtsh. u. Gynäk. **64:** 171, 1923. (7) *Schiffmann and Seyfert:* Arch. f. Gynäk. **127:** 708, 1925. (8) *Roques, Fred:* Proc. Roy. Soc. Med. **21:** 24, 1928. (9) *Spitz, H.:* Am. J. Clin. Path. **2:** 155, 1932. (10) *Lanos, J., and Busser, F.:* Bull. et mém. Soc. de chir. de Paris **25:** 134, 1933. (11) *Herberz, O.:* Monatschr. f. Geburtsh. u. Gynäk. **95:** 259, 1933. (12) *Schwarz, F.:* Bratisl. lekár. listy **14:** 19, 1934. (13) *Galasso, A., Sherman, B. G., and Burn, V. E.:* J. A. M. A. **102:** 1845, 1934. (14) *Bingham, E. M., and Templeton, W. W.:* California & West. Med. J. **41:** 330, 1934. (15) *Planson, V.:* Bull. et mém. Soc. de chir. de Paris **26:** 611, 1934. (16) *Weller, C. V.:* Am. J. Path. **11:** 281, 1935. (17) *Knoflach, J. G.:* Wien. klin. Wchnschr. **48:** 698, 1935. (18) *Enzer:* Arch. Path. **10:** 879, 1930. (19) *Palmén, A. J.:* Acta Chir. Scandinav. **62:** 310, 1927. (20) *Mazer and Goldstein:* Clinical Endocrinology of the Female, Philadelphia, 1932, W. B. Saunders Co., p. 181. (21) *Witherspoon, J. T.:* Arch. Path. **20:** 20, 1935.

304 WEST SEVENTY-FIFTH STREET

GRANULOSA CELL CARCINOMA

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THIS case is reported as an addition to the increasing list of granulosa cell carcinomas.

Mrs. A. M., fifty-two years of age, was admitted to the Jersey City Medical Center Nov. 24, 1931 with the diagnosis of metrorrhagia.

In May, 1931, the patient noticed uterine bleeding accompanied by backache. The bleeding was intermittently scanty or profuse without any definite cycle and persisted until admission to the hospital. The menstrual history was normal. She has one child living and well. Menopause occurred at the age of forty-seven.

Physical examination revealed nothing unusual, except an obese female with turgid and prominent breasts. The pelvis showed a hypertrophic cervix, rectocele, and a third degree prolapse of the uterus. The red blood count was 3,450,000, hemoglobin 65 per cent (Tallqvist), the white count 11,500 and the differential count, 81 per cent polymorphonuclears, 17 per cent lymphocytes, and 2 per cent large monocytes. All other clinical laboratory findings were negative.

Dec. 31, 1931, a total vaginal hysterectomy, perineorrhaphy and repair of the rectocele were done. Uneventful recovery followed the surgical intervention and the patient was discharged Jan. 23, 1932.

The pathologic report disclosed hypertrophy of the uterus with endometrial and cervical glandular hyperplasia. It is worth mentioning that the uterus measured 10 cm. from the fundus to the external os, 7 cm. in lateral diameter and 5.5 cm. in anteroposterior diameter.

Readmission: In January, 1933, the patient noticed a mass in her lower abdomen. On April 16, 1933, because of the progressive enlargement and of the intermittent abdominal pain, she was readmitted to the hospital.

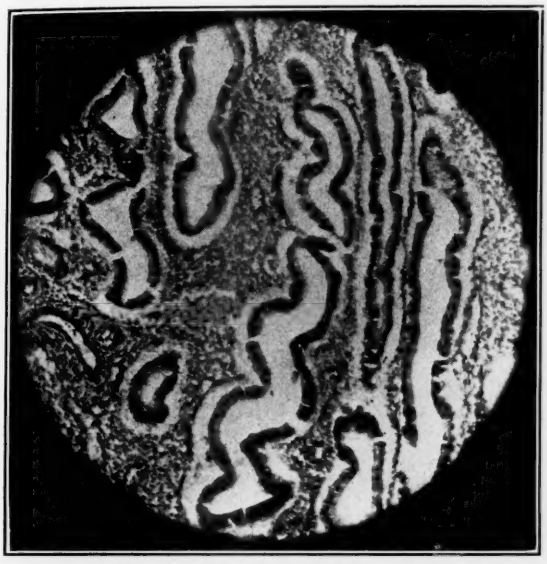

Fig. 1.—Endometrial proliferation of tortuous and dilated glandular acini (low magnification).

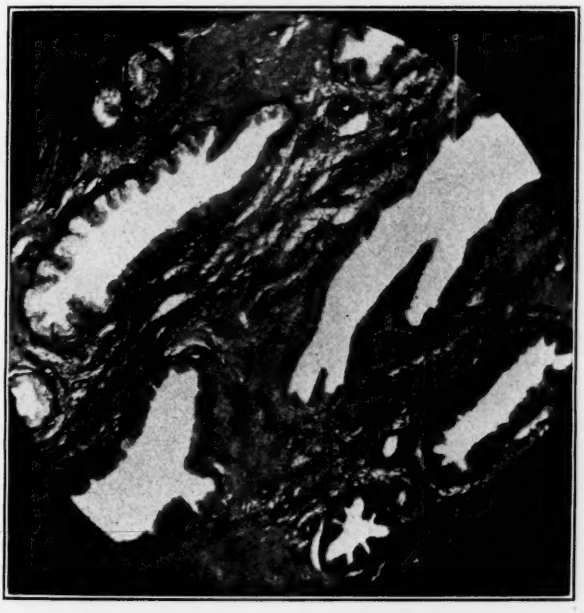

Fig. 2.—Cervical glands showing a typical hyperplasia (low magnification).

At this time, after no apparent loss of weight, the pelvic examination revealed a rather smooth oval-shaped mass arising from the right lower quadrant extending to the umbilicus. The red blood count was 3,920,000, hemoglobin 65 per cent,

Tallqvist, the white count 12,480, and the differential count 80 per cent polymorphonuclears, 14 per cent lymphocytes, and 6 per cent large monocytes; other laboratory work was essentially negative.

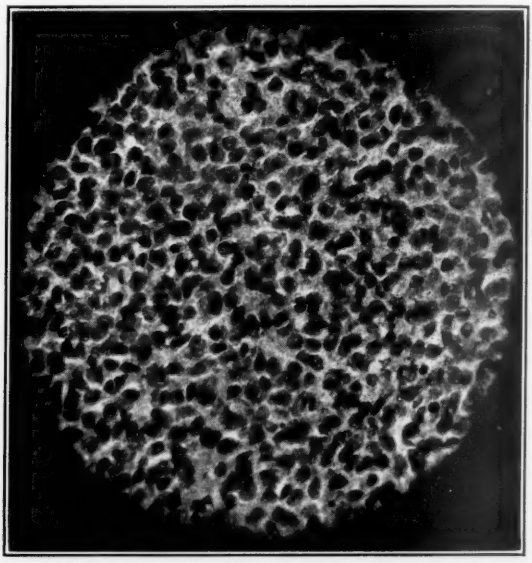

Fig. 3.—Solid mass of granulosa cell tumor (high dry magnification).

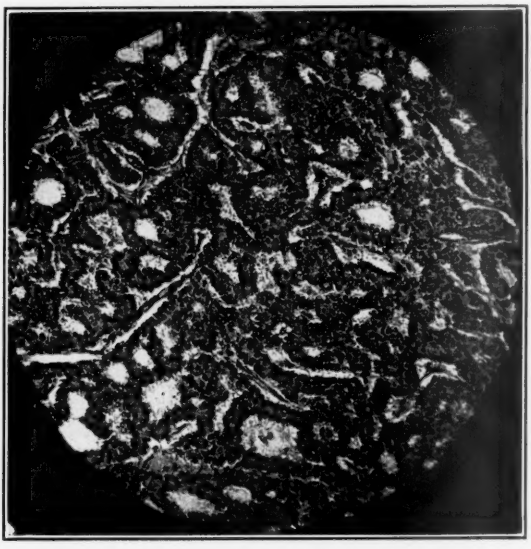

Fig. 4.—Folliculoma associated with cysts. Section taken at random (low magnification.)

A clinical diagnosis of ovarian cyst was made and on May 2, 1933, the patient was subjected to a right salpingo-oophorectomy with the delivery of a mass, the size of a honeydew melon.

Pathological Report: The tumor measured 26 by 22 by 16 cm. in its largest axes. The surfaces were smooth, grayish white and markedly lobulated. On section, the

exposed surfaces revealed numerous roughly nodular areas sharply separated by thick or thin fibrous septa. These areas varied from 0.3 to 5 cm.; their texture was coarse or finely granular and their color was pearly gray or yellow. Interposed in the bulk of the tumor were several hemorrhagic cysts varying from 0.2 to 8 cm.

The tube was without gross abnormality and microscopically showed an atropic mucosa with a spotty lymphocytic infiltration of the submucosa with moderate fibrosis of the muscularis.

After fixing in 10 per cent formalin, the tissue was stained with hematoxylin eosin.

Microscopic Description: Sections showed a fibrous or fibromyxomatous stroma invaded by well-defined nodular masses composed of large polyhedral cells devoid of cellular membrane, with a clear, granular foamy cytoplasm with centrally placed round or oval nuclei moderately dotted with chromatin granules. Nuclear vacuolization was often seen. The nucleoli were conspicuous. Mitotic figures were infrequently found. The epithelium had a varied arrangement. The bulk of the tumor

Fig. 5.—Folliculoma associated with cysts. Section taken at random (low magnification.)

was composed of solid masses of granulosa cells, although not infrequently, these cells were supported by a hyaline stroma. In places, the epithelium assumed a cord-like appearance which resembled the undifferentiated gonadal structures.

In other areas, a follicular arrangement of the epithelium, with simple or hemorrhagic cystic degeneration, was noted. Vascularity was poor and some of the medium-sized vessels manifested subendothelial proliferation, leading to partial or complete occlusion of the lumina.

CONCLUSIONS

1. Vaginal bleeding, in the absence of tumors of the uterus or cervix, should suggest, among other possibilities, a granulosa cell carcinoma.

2. Granulosa cell carcinomas, as a rule unilateral, have a low degree of malignancy and the prognosis, after removal, is good. (At the time of writing, our patient is still in good health.)

3. The hormonal influence of these tumors is typically illustrated by this case.

TUBAL PREGNANCY IN A CASE OF BILATERAL TUBAL IMPLANTATION*

With Inspection of Operative Site After Three Years

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FOR the past few years at Bellevue Hospital, we have been doing plastic surgery upon occluded oviducts according to the technic described and published by us in 1932.† We therefore believe this case report is of interest for the following reasons:

1. A celiotomy permitted a survey of the end-results of the tubal implantation technic.

2. The tubal patency persisted postoperatively for a period of years, and there was no evidence of contraction due to cicatrization of the newly created ostia in the horns of the uterus upon the implanted tubes.

3. Intrauterine gestation has occurred following plastic operations on the oviducts, as we reported, but the possibility of ectopic pregnancy must also be borne in mind; not primarily the result of the operation, but most probably of pathologic damages in the occluded tubes which remain from the original disease, if we are to accept the theory of infection as the main etiologic factor in tubal pregnancy.

Mrs. I. K., aged thirty-one years, was hospitalized because of severe right lower quadrant pain and backache of six months' duration. She was operated upon in February, 1932, for chronic adnexal disease and a retroverted, adherent uterus, with both adnexa prolapsed and adherent in the culdesac. No definite history of any previous infection could be obtained.

Operative Findings: Uterus retroverted, adherent in culdesac, with a fibroid, 1 cm. in diameter, on the fundus, 2 cm. from the right cornu. The omentum was adherent to its posterior surface. Both adnexa were prolapsed, the left being adherent; both ovaries appeared to be normal.

An intrapelvic tubal insufflation test disclosed that both tubes were occluded about 0.5 cm. from the cornu. Because the patient had never been pregnant, it was decided to perform a plastic operation upon the tubes. Therefore, both tubes were implanted into the uterus according to the technic referred to. An Olshausen suspension of the uterus was done. The small subserous fibroid was enucleated. Both adnexa were suspended, using the Poole technic.

The convalescence was uneventful.

Three weeks after discharge from the hospital, the uterus was in good position and no adnexal pathology was palpable. A transuterine tubal insufflation demonstrated the patency of the tubes.

For the following seventeen months the patient was symptom free, and her menses were regular. She then had an amenorrhea of seven weeks' duration. After strenuous daily indulgence in swimming during this entire period of amenorrhea she started to bleed, and her local physician diagnosed the case as one of intrauterine pregnancy with abortion and treated her palliatively, no curettage being deemed necessary.

*Presented at a meeting of the New York Obstetrical Society, February 11, 1936.

†Holden, F. C., and Sovak, F. W.: Am. J. Obst. & Gynec. 24: 684, 1932.

After this abortion her menses again were regular, every twenty-eight days, with no associated pain, until one year later (about July 18, 1935), at which time following a six weeks' amenorrhea, she complained of a gradually increasing vaginal bleeding accompanied by occasional abdominal cramps of fourteen days' duration. On Aug. 2, 1935, the abdominal cramps became severe and localized in the right lower quadrant, associated with vomiting and a feeling of weakness, but no fainting.

Examination at this time revealed marked tenderness and slight rigidity of the lower abdomen, with a tender mass palpable in the right lower quadrant just above Poupart's ligament. Vaginally there was a dark, bloody discharge; the cervix was in good position; the fundus well anterior, slightly enlarged and soft. There was extreme tenderness in the uterosacral region, and a fixed, tender mass in the right adnexal area about 8 by 10 cm., extending into the culdesac. Pulsating vessels were also palpable. The left adnexal region was negative.

Clinical Findings: Hemoglobin 55 per cent (Sahli), erythrocytes 2,800,000, with 12,000 leucocytes, differential count 70 per cent polymorphonuclear cells, 15 per cent lymphocytes, and 5 per cent monocytes. The blood pressure was 100/80. The temperature was normal, but the pulse was 105.

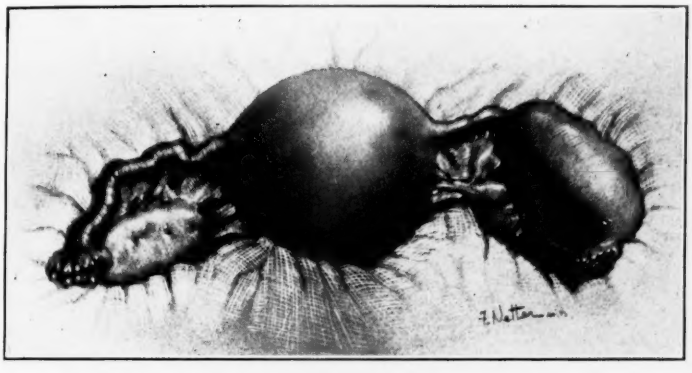

Fig. 1.—Left implanted tube appears practically normal although slightly shorter. Right tubal pregnancy in fimbriated extremity of tube. Left tube found patent by intratubal insufflation test.

A diagnosis of tubal abortion was made and a celiotomy was advised.

Operative Findings: Many free and partially organized blood clots were found in the peritoneal cavity. The right tube was edematous, bluish and distended in its outer half by a mass 3 by 6 cm., with free blood oozing from its fimbriated extremity. The right ovary showed a corpus luteum cyst and was adherent to the tube. The left tube and ovary appeared to be grossly normal and well suspended by the previous Poole technic. The uterus was well anterior, slightly enlarged and soft.

Operative Technic: The old suprapubic scar was excised. The blood and blood clots lying free within the peritoneal cavity were removed and a right salpingectomy was performed. The left tube was then insufflated and found to be patent; no definite cicatricial tissue was identified about the left cornual portion of the uterus, and the implanted tube appeared as if it were a tube in its normal position except that it seemed to be slightly shortened. No evidence of adhesions or kinking was present.

The patient had a mild postoperative reaction and was discharged on the tenth day.

Pathological Report: "Gross specimen consists of a distorted tube about 8 cm. in length and 3 cm. in diameter in its entire outer half, with thickened, congested, and edematous walls. The fimbriated end was retracted. Accompanying the specimen were remnants of blood clots which appear to be partly organized.

"Microscopic section of the tube shows the walls congested, edematous and hemorrhagic, showing abundance of cellular infiltration mostly of polymorphonuclear leucocytes which is most abundant in the mucosa. The tubal blood clot shows groups of decidual cells and chorionic villi."

Diagnosis: Tubal ectopic gestation.

CONCLUSIONS

Although ectopic tubal pregnancy may ensue in oviducts that suffered from infection, normal intrauterine gestation occurs often enough to justify plastic operations upon the tubes.

755 Park Avenue

PREGNANCY AND DELIVERY AT TERM FOLLOWING RECONSTRUCTION OF OVIDUCTS*

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Mrs. M. C. H., aged thirty-three years, married four years; chief complaint: sterility. Past medical history: diphtheria and typhoid fever. Past surgical history: 1921 laparotomy for acute appendix with abdominal drainage. This was followed ten days later by a posterior colpotomy with drainage of a complicating pelvic abscess. Menstrual history: onset thirteen years, twenty-eight-day interval, duration seven days, moderate flow with very little pain. The physical examination was negative except for a firm McBurney's scar. Normal marital introitus, Skene's ducts and Bartholin's glands negative, cervix in axis and canal clean, uterus normal size and in third degree retroversion, not replaceable. No adnexal nor parametrial pathology palpable.

Several attempts at tubal insufflation showed no gas passing through at pressure up to 200 mil. of mercury. Lipiodol examination was done June 20, 1933. This showed both tubes closed at the fimbriated extremities and no lipiodol escaped into the peritoneal cavity subsequent to the test.

The husband was thirty-three years old, height 5.7, weight 159, general health excellent. Sperm examination showed the number to be adequate and of good motility. Morphologic examination showed 90 per cent normal heads, indicating the sperm to be well within the normal limits of fertility.

A laparotomy was done July 12, 1933, at the French Hospital. Operative findings: The uterus was adherent in retroversion, and both adnexa were buried behind the uterus. The left tube was transformed into a hydrosalpinx which still contained some lipiodol. The left ovary was normal. The right tube and ovary formed a firm inflammatory mass, which was densely adherent to the culdesac and pelvic peritoneum, the ovary being enlarged to three times its normal size. Both tubes were closed at the fimbriated extremities. Many adhesions were present at the site where the appendix had previously been removed.

Operative technic: A phimosis operation was done on the end of each tube according to the Bonney-Sovak technic, leaving both tubes patent at the end of the operation. A Webster-Baldy suspension of the uterus and Poole's suspension of

*Read before the New York Obstetrical Society, February 11, 1936.

both ovaries were done. The abdomen was closed without drainage. On the third postoperative day, a Rubin test was done and gas flowed through the tubes at 20 mm. of mercury. From the fifth postoperative day until discharge, daily Elliott treatments were given. The patient had a smooth postoperative course and was discharged on the fifteenth day.

A Rubin test done two months after the operation showed both tubes to be of normal patency. For eight months after the operation the husband was away on business. The patient became pregnant six months after his return. She was delivered at full term of a normal male child Sept. 30, 1935, and had a smooth postpartum course.

DISCUSSION

DR. THOMAS C. PEIGHTAL.—The percentage of subsequent tubal patencies in any series depends largely upon the choice of cases suitable for this operation. Even on an active service the number of such cases is not large. During the past three years on the Gynecological Division of the Roosevelt Hospital in only fifteen instances has the condition of the tubes been found favorable for implantation into the uterine cornua. This has been done by the Sovak method and in approximately 80 per cent subsequent patency has resulted.

Unfortunately in none of these cases has pregnancy ensued. The physiologic efficiency of these reconstructed tubes must necessarily be greatly reduced by the preexisting mucosal damage so that the obtaining of patency is only part of the problem in overcoming the sterility. Based upon patency alone, these operations have achieved a higher degree of success in our hands than any reconstructive surgical procedure heretofore practiced, and on this basis alone can be recommended to patients with assurance. However, if the ultimate success of these operations must be judged by the pregnancies obtained, it would seem that the problem of sterility from chronic salpingitis is only partly solved.

DR. ISIDOR C. RUBIN.—In my experience, success comes more readily in the cases where the fimbriated ends of the tubes have become agglutinated from an infection gravitating downward from a suppurative appendicitis. I have had several such cases where the tubes, being sealed like a phimosis, have yielded to an insufflation pressure of from 160 to 200 mg. of mercury. Pregnancy has occasionally taken place as a result of that treatment. The cases of gonorrheal infection, however, where the occlusion takes place at the isthmic portion, are not so favorable.

Success is more likely to follow a combination treatment which considers not only the mechanical occlusion but also the fact that the tubes themselves still contain residual inflammation.

I would like to ask Dr. Sovak whether he has met with intrauterine gestation continuing to term after the tubal implantation operation. I myself have done this operation several times and have had no such success.

DR. H. DAWSON FURNISS.—There is a point in the technic of the implantation of the tube that I think serves to simplify the operation. This consists in passing a Reverdin needle through the fundus into the end of the cork borer after the borer has reached the uterine cavity. When the borer is removed the needle will be found protruding from the tunnel that has been cut. A suture that has been passed through the end of the tube is threaded into the needle. Withdrawal of the needle and traction on the suture will pull the tube into the uterine cavity.

DR. SOVAK (closing).—As we know, many other factors besides the mechanical ones enter into the question of sterility. Bilateral occlusion of the tubes, however, stigmatizes the woman as being absolutely sterile instead of relatively sterile.

In answer to Dr. Rubin, I would state that in our first case of implantation done at Bellevue Hospital, the patient became pregnant. This case was one of the first series that we reported.

At the Bellevue Hospital out of 15 implantation cases, we could follow only 10, and of these 10, 6 were found to have patent tubes. The cases that Dr. Holden and I reported tonight were private cases. If we follow only our private cases, the results will show marked improvement over the hospital series.

DR. HOLDEN (closing).—One should not consider operating for occlusion of the tubes without definite information as to the general health of both wife and husband, including a morphologic sperm count. Our statistics demonstrate that in over one-third of the sterile couples, the husband is the cause of the infertility.

Within one year we have seen three doctors' wives, one with secondary and two with primary sterility, in all of whom the husbands had poor sperm specimens. After these husbands had been put in better condition, the wives became pregnant, two delivered full-term healthy babies, and the third had a six months' miscarriage. Many miscarriages and congenitally deformed children can be traced to poor sperm.

CHORIONEPITHELIOMA COMPLICATED BY SEPTICEMIA*

ROLAND S. CRON, M.D., F.A.C.S., MILWAUKEE, WIS.

A WHITE multipara, aged forty-one years, married, gave a history of pericarditis during childhood. Her menstrual history was essentially normal. She was married at twenty-six years and has three children living and well, the youngest nine years of age.

There were at least two uncomplicated abortions. In June, 1935 the last normal menstrual period occurred. Six weeks later profuse bleeding started, but there was no evidence of the patient having been pregnant. A show of blood continued throughout July and August but in September this stopped for about two weeks. The husband reported that a pelvic examination in August showed the organs to be in normal condition. Late in September the bleeding recurred so that early in October she was again examined and a small mass was palpated in the region of the right adnexa. Subsequently I learned that a Friedman test was positive on October 4.

My first contact with the patient was on October 7. She had no complaints except slight backache and occasional bloody discharge. Examination was essentially negative, except for the palpation of a soft cystic mass the size and shape of the average thumb located in the right broad ligament region extending down to about the level of the tip of the cervix. A diagnosis of broad ligament cyst, ectopic pregnancy, or chorionepithelioma was ventured. Because of the age of the pregnancy and freedom from pain the diagnosis of ectopic was ruled out. The latter diagnosis, namely chorioma, was considered most seriously.

Diagnostic dilatation and curettage were immediately advised, but the patient did not enter the hospital until October 14. The small uterus was deeply and carefully curetted and yielded only a very atrophic endometrium in the early proliferative phase. The mass in the right vaginal wall appeared slightly bluish and vesicular and suggestive of dilated veins. A piece of tissue 2 by 1 cm. was excised. Unusually active bleeding occurred which was controlled only by deep sutures. Again the diagnosis of chorionepithelioma was seriously considered, but the pathologist could find no evidence of malignancy and reported the following: "Almost complete disappearance of squamous epithelium, inflammatory reaction, congestion but no decidual reaction."

*Read at a meeting of the Chicago Gynecological Society, January 17, 1936.

The convalescence was uneventful. The patient returned to her home on the fifth postoperative day after an afebrile convalescence. Five days later a very brisk hemorrhage occurred necessitating packing, hospitalization and resuturing of the incised area in the vagina. The tissue had sloughed and the area had increased in size to about 2 × 6 cm. Spurting arteries were visible. These were ligated and the edges of the sloughed area were freshened and resutured. Eight transfusions were subsequently given.

In one extremely tiny bit of all of this tissue we were able to demonstrate a typical malignant chorioma with marked polymorphonuclear infiltration and hemorrhage.

A Friedman test was markedly positive at this time as was also one diluted 1 to 10 times. However, only one ovary in each rabbit showed the typical hemorrhagic follicles.

Within nine hours following the secondary closure, a fifteen-minute chill occurred followed by daily or twice-daily chills, and elevation of temperatures as high as 107.6° rectally. The pulse varied from 80 to 140. A blood culture was positive for staphylococci. The blood counts both red and white were high but both gradually

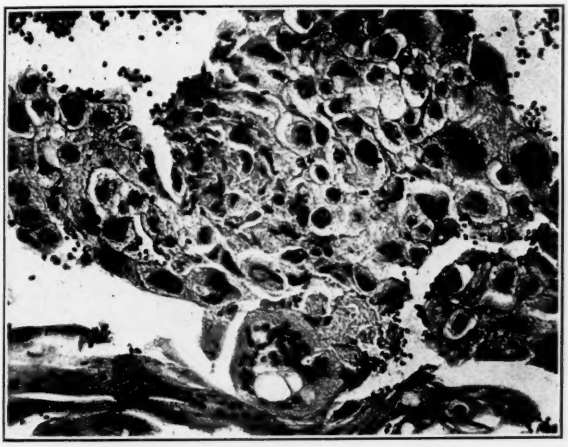

Fig. 1.—Tissue from broad ligament showing typical malignant chorioma with polymorphonuclear infiltration.

fell. Convalescent serum and pentose nucleotide were administered. The blood sedimentation velocity was 31, not unusually rapid. There was a severe pyuria.

Slight to moderate vaginal bleeding with a fetid discharge continued necessitating daily packing moistened with 5 per cent mercurochrome. The patient became icteric and toxic.

Consultants agreed that temporarily at least control of the septicemia was most important and that treatment of the chorionepithelioma should be held in abeyance. On the eighth day following the secondary closure a profuse hemorrhage recurred necessitating an attempt at a second resuturing or ligation of the internal iliac vessel. At this time the slough had become so deep it was impossible to reach its apex. The edges were whipped together with great difficulty due to the friable necrotic tissue. However, the bleeding was controlled but again the temperature rose to 108° and within twenty-four hours another severe hemorrhage occurred resulting in death. No attempt was made to ligate the iliac artery due to the extremely serious condition of the patient and apparent rapid extension of the growth.

An autopsy showed an old fibrous scar at the apex of the left ventricle, fresh infarcts in the spleen and two nodules in the right upper lobe of the lungs. These

were 1 cm. in diameter and appeared as soft bluish red masses. Microscopic sections showed that they were thrombosed vessels with metastatic tumor cells, polymorphonuclear leucocytes and tissue which resemble chorionic villi (Fig. 2). The uterus, ovaries, and tubes appeared normal except for a small follicle cyst in the right ovary. The endometrium of the small uterus was very atrophic.

In the right broad ligament there was a mass the size of a baseball. It reached from below the tube to halfway down the vagina. The wall was made up of sloughing, necrotic, hemorrhagic tissue with marked induration. There was extensive thrombosis into the common iliac vein. A thorough microscopic study of this tissue showed no tumor cells.

This case presents many interesting problems. There is the original diagnosis of ectopic pregnancy or chorionepithelioma. The former was never seriously considered because of the duration of the pregnancy and the small size of the mass as well as the absence of pain. Had this been an ectopic in which the fetus had died, the Friedman test should have become negative. It must be admitted that a broad ligament cyst was seriously considered, especially when the uterine curettings and vaginal biopsy showed no evidence of a chorioma.

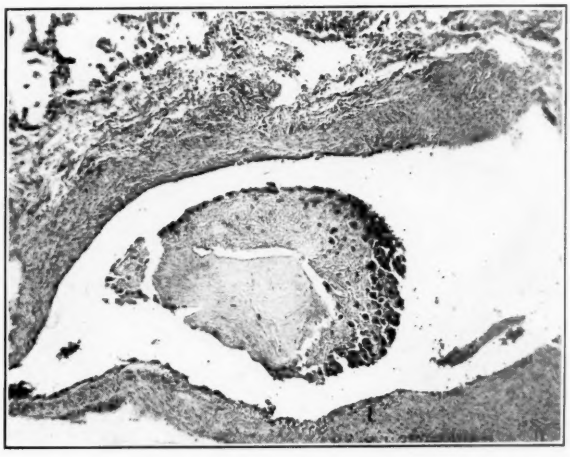

Fig. 2.—Chorioma cells in pulmonary vein.

The absence of tumor cells in the uterine curettings, although the curettage was deep enough to obtain uterine muscle, shows the fallacy of ruling out the diagnosis of chorioma by this method. The reason the lesion was not recognized by study of the biopsy material was probably due to the fact that enough tissue was not obtained. The growth was so destructive that all we obtained was evidence of inflammation, hemorrhage, and necrosis.

The severe reaction following the secondary closure was probably due to the absorption of bacteria and necrotic material directly into the blood stream. This made it appear inadvisable to treat the chorioma with radium or x-ray. Of course, surgery was not considered because of the location of the lesion and condition of the patient. Might not it have been advisable even in spite of the bacteremia to have x-rayed this patient?

An interesting feature of the Friedman tests was the reaction to the undiluted and diluted specimens. Only one ovary in each of two different rabbits showed hemorrhagic follicles. This has been observed by others and may be the result of an antihormone, a lack of response on the part of the ovary or a deficiency of hormones. It is difficult to believe that the same ovary in two different rabbits

should be refractory to prolan. Certainly there was sufficient potency, for a dilution of 1-10 produced moderately large blood points. There must be some other explanation.

The most shocking thing about the entire case was the absence of involvement by the tumor of the pelvic organs. Did this lesion reach the broad ligament through the lymph or blood vessels? It probably did so, remained inactive and then took on a very rapid growth months following the termination of a very early pregnancy. Chorionepitheliomas have been found in the testicle, but I doubt if this one had any such anlage. Not until the tumor cells were found in the blood vessels of the lungs did we feel certain that our original diagnosis was correct.

425 East Wisconsin Avenue

FULL-TERM NORMAL PREGNANCY FOLLOWING THE USE OF ONE THOUSAND MILLIGRAM HOURS OF RADIUM FOR MENORRHAGIA*

Herbert E. Schmitz, B.S., M.D., F.A.C.S., Chicago, Ill.

A COLORED female, twenty-three years of age, presented herself at the Cook County Hospital in March, 1935, because of a menorrhagia of one year's duration. Menstruation had begun at the age of twelve years, was always of the twenty-eight-day type lasting five days. Pain or clots had never been experienced. For the year previous to admission the duration of menstruation had been twelve days, very profuse and large clots were passed during the entire period. The previous obstetric and marital history was that she had been married one year and then separated. During the year of married life she had one normal pregnancy resulting in a normal viable fetus. No pregnancies had followed.

Upon admission to the hospital an examination showed a negative introitus, uterus firm but tender in the region of the adnexa, sacral nerve roots and uterosacral ligaments tender. One thousand milligram hours of radium element was advised and the radium inserted on March 11, 1935.

July 15, 1935 the patient presented herself to the Tumor Clinic of the Cook County Hospital with the following history: Last menstrual period Feb. 21, 1935 lasting for twelve days. Following this, radium was inserted on March 11, 1935, and since this time no menses had been noted. Examination at this time revealed an apparently normal colored female. Breasts were enlarged and contained colostrum. Abdomen was negative except for a smooth mass palpable above the pubes. The introitus was negative. Cervix in the midplane and softened. Os round and closed. Fundus size of large grapefruit, smooth but softened. The adnexa were negative. A diagnosis of pregnancy was made. The Friedman test was positive. The Wassermann and Kahn reactions were negative.

The prenatal course was uneventful, life being felt on Aug. 1, 1935. A roentgenologic study Oct. 18, 1935 showed one baby in abdomen with the breach in the pelvis and the spine on the left side. On Dec. 2, 1935, another roentgenogram showed the head in the pelvis and the spine on the left side anteriorly.

Labor began at 5 A.M. on Jan. 2, 1936 and ended Jan. 3, 1936. Duration of the first stage was twenty-two hours; of the second stage, one and one-half hours, and of the third, twenty-five minutes, a total labor of twenty-four hours. The membrane ruptured at 4 P.M. Jan. 2, 1936. It was a normal left occiput anterior. Patient was discharged on Jan. 10, 1936.

The baby weighed 5½ pounds and was perfectly normal in all respects and on discharge from the hospital had regained its normal birth weight.

*Read at a meeting of the Chicago Gynecological Society, January 17, 1936.

UNRUPTURED INTERSTITIAL PREGNANCY*

BEATRICE E. TUCKER, M.D., CHICAGO, ILL.

INTERSTITIAL pregnancy is sufficiently rare to merit the report of the following case. Mrs. F., aged twenty-eight years, was first seen in the office, Dec. 24, 1935. The chief complaints were: intermittent attacks of profuse vaginal bleeding since November 2 and cramplike pain in the left lower abdomen.

The patient had been married three years and had practiced birth control until September, 1935. At this time she wished to become pregnant. Her menstrual periods had always been very irregular, occurring from sixty to ninety days apart, and for the first two days of each period she had been confined in bed with severe abdominal cramps. The last menstrual period was September 1. The surgical and venereal histories were negative. Five years ago she had an attack of nephritis.

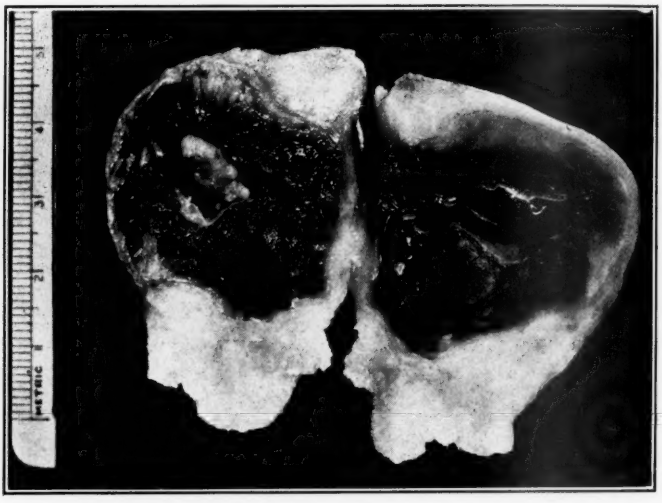

Fig. 1.

The onset of the present difficulty was November 2, sixty days following the last period. At this time she had profuse vaginal bleeding with severe cramplike pain in the left lower quadrant, referred to the left thigh. She flowed heavily for seven days and passed clots at times as large as hens' eggs. She was treated for abortion. However, intermittent attacks of more or less profuse vaginal bleeding accompanied with left-sided pain recurred throughout November and December. On December 24 she was referred to me.

At this time general examination was negative except for slight tenderness over the left lower quadrant. The positive findings on pelvic examination were a questionable softening of the cervix and slightly enlarged uterus with a mass about 6 cm. in diameter projecting upward from the left horn. This mass was tense, hard, and tender. A tentative diagnosis of cornual pregnancy or degenerating fibroid was made. The patient was immediately hospitalized for observation.

Upon admission the temperature, pulse, and respiratory rate were normal. The HB 70 per cent, R.B.C. 3,900,000, and W.B.C. 9,200. The urine showed an occa-

*Read at a meeting of the Chicago Gynecological Society, January 17, 1936.

sional hyaline cast. The patient was observed forty-eight hours. She had no vaginal bleeding during this time but complained of some discomfort in the left lower quadrant, and this pain was sticking in character and referred to the left thigh.

On December 26 an exploratory laparotomy was done. The uterus was found to be normal in size. A grayish pink, tense mass, 5 cm. in diameter, jutted upward from the left horn. Both ovaries were apparently normal. The tubes were slightly hyperemic.

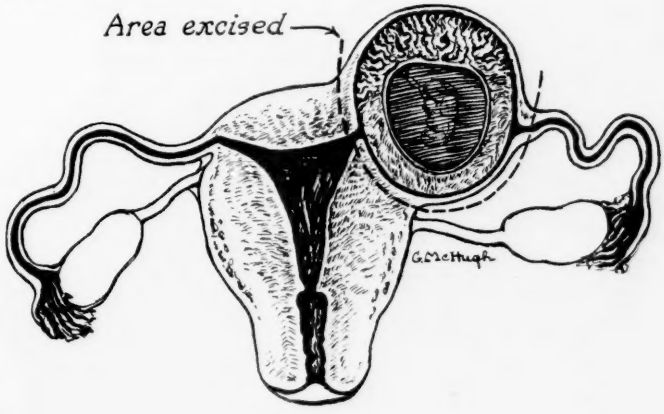

Fig. 2.

The mass was excised by removing a wedge-shaped piece of the uterus and severing the tube. The severed end of the left tube was sewed into the left horn of the uterus and the uterine wall was closed.

The specimen was opened and revealed a fetus 1 cm. long, lying in a gestation sac which dilated the interstitial portion of the tube.

The patient ran a low-grade temperature, from 99-100.6° for five days following the operation. Profuse vaginal bleeding occurred for five days and this ceased after four daily injections of 1 c.c. of antuitrin-S. On the tenth day she was dismissed from the hospital in good condition.

8 South Michigan Avenue

Kottneier, H. L.: Results Obtained With Thymophysin in Cases of Uterine Atony, Acta obst. et gynec. Scandinav. 14: 382, 1934.

The author reviews the literature on thymophysin and reports his experience with this drug in 163 cases of primary and secondary uterine inertia. Comparing the morbidity and mortality of both mother and child in these cases with a corresponding number of cases of inertia where no oxytocic drugs were administered, he finds that the outlook for the mother and baby was better in the cases where thymophysin was used. He also found that the drug resulted in a decrease in the number of dangerous obstetric operations. On the other hand, thymophysin may result in asphyxia of the child and also the mothers may show untoward reactions. Because of these dangers the author recommends that thymophysin be used only in cases of uterine atony. Not more than 0.5 c.c. should be given at any one time. He could not find any appreciable increase in blood pressure due to thymophysin. The drug is not effective in cases of exhaustion nor is it useful to induce labor. It is ineffective in 10 to 15 per cent of the cases where labor has definitely started. These cases, however, are the ones which should have received the drug earlier in labor.

J. P. Greenhill.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF FEBRUARY 11, 1936

The following case reports and paper were presented:

Pregnancy and Delivery at Term Following Reconstruction of Oviducts. Dr. Frederick C. Holden. (For original article, see page 346.)

Tubal Pregnancy in Case of Bilateral Tubal Implantation. Dr. Francis W. Sovak. (For original article, see page 344.)

Some Points in the Treatment of Endometrial Hyperplasia by Progesterone Therapy. Drs. Karl M. Wilson, and C. A. Elden. (For original article, see page 194.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF JANUARY 17, 1936

The following case reports and papers were presented:

Unruptured Interstitial Pregnancy. Dr. Beatrice E. Tucker. (For original article, see page 352.)

Full Term Normal Pregnancy Following the Use of 1.000 mg. hr. of Radium for Menorrhagia. Dr. Herbert E. Schmitz. (For original article, see page 351.)

Chorionepithelioma Complicated by Septicemia. Dr. Roland S. Cron. (For original article, see page 348.)

A Study of Fibromyomas of the Uterus With Respect to the Endometrium, Myometrium, Symptoms, and Associated Pathology. Drs. A. E. Kanter, A. H. Klawans, and C. P. Bauer. (For original article, see page 183.)

The Le Fort Colpocleisis. Dr. Fred L. Adair and Dr. Laura DaSef. (For original article, see page 218.)

Acute Nephritis and Pregnancy. Dr. W. J. Dieckmann. (For original article, see page 227.)

Cervicitis and Endocervicitis in Relation to Gynecologic Symptomatology. Dr. Howard J. Hollaway. (For original article, see page 304.)

Department of Reviews and Abstracts

Conducted by Hugo Ehrenfest, M.D.

Selected Abstracts

Eclampsia and Other Toxemias of Pregnancy

McIlroy, Louise: The Toxemias of Pregnancy. I. Clinical and Biochemical Investigation, Lancet 2: 227 and 291, 1934.

Since only six physiologists have taken particular interest in the study of human metabolic function in pregnancy, obstetricians have had to do most of these studies. Toxemias are the second most frequent cause of maternal deaths and produce damages beyond means of estimation. It is impossible to indicate in any way the number of fetal and neonatal deaths as the result of toxic conditions in the mother.

The ovum is the primary etiologic factor. If the ovum fits into its surroundings harmoniously, all goes on to a happy ending. If the adjustment fails, the ovum acts as a parasite and tends to poison its hostess. Theories and predisposing causes of toxemia are mentioned. The diet plays an important part, especially the amount of salt. Salt should be restricted if any untoward symptom develops. Obese or heavy women should keep their weight down, and those who grow too rapidly must also restrict their diet. To combat the retention of tissue fluids, salt must be restricted. Reasonable walks of two to three miles in fresh air are urged.

The toxemias are divided into the hepatic and nephritic groups. The former are often acute and include fulminating eclampsia, acute yellow atrophy, or severe vomiting of early pregnancy. The liver is concerned with the neutralization of protein substances, and when the organ is injured, this function is limited or destroyed. The nephritic type covers two groups: in the one the kidney appears to recover and remains healthy until a second pregnancy, known by some as the low reserve kidney. The other group comprises chronic nephritis. Even with these divisions it is often difficult to make a differential diagnosis.

Some discussion is advanced for toxemia as a deficiency disease. The substances considered are calcium, vitamin D, glycogen, iron, manganese and magnesium, iodine, and even insulin.

H. Close Hesseltine.

McIlroy, Louise: The Toxemias of Pregnancy. II. The Significance of Symptoms and Their Treatment, Lancet 2: 345, 1934.

Emphasis is placed upon treating the patient and not the disease. Prevention is obviously the best approach, even though there are a few fulminating toxemias. In general, the diet should avoid excessive or unsuitable foods. The elimination of harmful substances by physiologic rest and the stimulation of those organs concerned with excretion is necessary therapy.

The diet should be, as far as is expedient, that to which the patient is accustomed. It should be plain mixed variety containing ample vitamins, minerals, and not excessive meat. Constipation should not be treated by cathartics. For morning vomiting confine the patient in bed, allay worries and unusual mental and physical stimuli. For the first twenty-four to forty-eight hours permit only water, glucose, and fruit juices. If vomiting occurs, wash the stomach, use sedatives as necessary, and increase diet as tolerated. Heart burn is best treated by dilute hydrochloric acid (15 to 30 drops) during meals. Headaches should not be overlooked.

Hypertension, if it does not respond to treatment, should be treated by termination of pregnancy. Rapid reduction in hypertension by medication is contraindicated. Venesection has an important place in the treatment.

Ocular disturbances must be carefully interpreted and, with presence of hemorrhages, separation of retina or retinitis, termination is indicated.

Anemia is due principally to vitamin and iron deficiency and should be combated. Foods containing iron are to be urged. Blood transfusion may be necessary in severe anemia, toxemia, shook, and sepsis. The treatment of antepartum hemorrhage depends upon the conditions present. Postpartum hemorrhage is treated best by prevention.

Gas and oxygen is a safe anesthetic.

The urine and blood must be examined, and for kidney function tests uric acid is a finer test than urea. Antenatal and postnatal care are very important and are avenues where improvement may be made in obstetrics.

H. CLOSE HESSELTINE.

Fairbairn, John S.: Prevention and Prognosis of the Late Toxaemias of Pregnancy, Brit. M. J. **2:** 531, 1935

Late toxemias are those occuring after the twenty-eighth week of pregnancy. A true albuminuria and hypertension are constant features. Frequently edema, headache, vomiting, insomnia, cramps, jaundice, or polyneuritis are associated symptoms.

In the field of prevention, strict antenatal observation, including dietary supervision, especially the administration of carbohydrates, calcium and vitamins, is essential. Foci of infection must be searched for and treated. Early signs of disordered metabolism must be recognized and remedial measures instituted. Bed rest, magnesium sulphate, and alkalis are advisable early in toxemic manifestations. Improvement under this regime justifies continuation of pregnancy; failure to improve is an indication for termination.

In spite of the large number of preeclamptic patients who are saved from convulsions by thorough antenatal care, the actual death rate from eclampsia from 1921 to 1931 and since was unaltered. However, the prognosis for the toxemic patient is somewhat better than formerly. Strict supervision is essential. The prognosis of eclampsia depends upon the number and frequency of convulsions. Coma, fever, and jaundice lend a graver outlook. The danger to the fetus is much less in the nonconvulsive than in the convulsive toxemias, and less than in the chronic nephritic conditions.

F. L. ADAIR AND S. A. PEARL.

Courtois, J., and Lecoq, R.: Toxemias of Pregnancy and Nephritis, Gynécologie **34:** 665, 1935.

Among the true toxemias the authors include hyperemesis gravidarum, eclampsia, obstetrical shock, hydatidiform mole, uteroplacental apoplexy, and post-

operative toxic infectious shock. Excessive vomiting of pregnancy is above all a syndrome of malnutrition, hypotension, and hypochloremia in which an abnormality in intestinal function plays a large part.

Eclampsia or convulsive and hemorrhagic toxemia is essentially a syndrome of plethora, hypertension, and hyperchloremia with acidosis.

Obstetric shock manifests itself particularly in plethoric women and may be prevented.

In addition to the true toxemias, the authors list a number of "paratoxemias" such as polyneuritis of pregnancy, chorea gravidarum, tetany, osteomalacia, pernicious anemia, icterus gravis, the toxic dermatitis, cardiac accidents and severe forms of the grip.

Nephritis may give rise to symptoms of toxemia. Occasionally it may terminate in eclampsia. Hypertensive nephritis may provoke uteroplacental apoplexy, the hemorrhagic form of eclampsia or obstetric shock.

J. P. GREENHILL.

Strauss, M. B.: Observations on the Etiology of the Toxemias of Pregnancy, Am. J. M. Sc. **190:** 811, 1935.

In 20 cases of nonconvulsive toxemia of pregnancy the average osmotic pressure of the plasma proteins was 215 mm. of water, in 10 cases of eclampsia it was 175 mm. and in 20 normal pregnant women with adequate diets it was 258 mm. In 15 normal pregnant women who had partaken of diets low in protein, the average osmotic pressure of the plasma proteins was 232 mm. of water.

The average venous pressure in 20 normal pregnant women during the last two months of pregnancy was 10 cm. of water (range 3 to 18 cm.), and in 20 patients with nonconvulsive toxemia of pregnancy 13.3 cm. (range 8 to 20.5 cm.), values which are at least twice as high as average figures for normal nonpregnant subjects.

The dietary histories of 20 toxemic pregnant women showed a low protein intake, probably less than 50 gm. per day, frequently over a period of years.

Fifteen women suffering from toxemia of pregnancy were treated by means of a diet containing 260 gm. of protein, 150 gm. of carbohydrate, and 70 gm. of fat. Ten also received parenteral injections of a vitamin B_1 concentrate and solution liver extract-Lilly (N. N. R.), the latter because of its content of the pellagra-preventive portion of the vitamin B complex. Each of the 15 women showed a loss of weight readily attributable to decrease of occult or gross edema, together with a gradual disappearance of the signs and symptoms of toxemia. No fetal mortality occurred after treatment had been instituted.

Five similar pregnant women suffering from toxemia were treated by means of a diet of approximately equal caloric value, containing 20 gm. of protein, 400 gm. of carbohydrate, and 65 gm. of fat. No significant loss of gross or occult edema occurred. Two of the patients became decidedly worse during a period of two weeks.

It is believed that a manifestation of toxemia of pregnancy is water retention. This water retention probably occurs as a result, among other factors, of a lowered osmotic pressure of the plasma proteins, usually in the presence of an increased venous pressure. The results recorded in this paper suggest that a restricted dietary intake of protein in pregnancy is harmful, and that no injurious consequences follow the administration of high protein diets to women with toxemia of pregnancy. The beneficial results observed in these patients may well have been due to the large protein intake and to the parenteral administration of accessory nutritional factors.

J. THORNWELL WITHERSPOON.

Rowe, A. W., McManus, M. A., and Riley, G. A.: The Toxemias of Pregnancy, J. Lab. & Clin. Med **19:** 923, 1934.

This study is concerned with protein metabolism as evidenced chiefly in the levels of blood and urine nitrogen. The results are compared with a previously studied normal group of primiparas. This toxemic group consisted of older women, one-third of whom were in their first pregnancy. The authors summarize their work as follows: Pregnancy causes a lowering of the nitrogenous constituents of the blood, uric acid excepted, which is less marked in cases of toxemia as the renal element is an opposing influence. Termination of pregnancy initiates a return to normal levels, the latter being less rapid in the toxic group. Restoration to normal blood levels follows rapidly on the termination of the pregnancy in both studied groups. No evidence is forthcoming in this study that repeated fetation led to results differing from those characterizing primiparas.

W. B. SERBIN.

de Snoo, K.: Renal Function in Pregnancy Toxicosis and Eclampsia, Monatschr. f. Geburtsh. u. Gynäk. **97:** 253, 1934.

It is the opinion of de Snoo that in the simple toxicosis of pregnancy there is rarely any marked disturbance in the renal function. Likewise, in cases of chronic hypertension, even in those with outspoken uremic manifestations, the kidney function is little if at all deranged in most cases. However, in women who have recovered from eclampsia, there are serious disturbances in the function of the kidneys both as regards the output of fluids and the urinary products. In these women the urinary output is more quickly recovered than the elimination of proteins. The accumulation of proteins in the blood is harmless, and, therefore, the prognosis is dependent more upon diuresis than upon the nitrogen content of the blood. In many cases of eclampsia the renal function is entirely normal before the onset of convulsions. The effect of convulsions on the kidneys is not specific because the same effects may be observed in patients without convulsions. The renal disturbances are dependent upon vasomotor abnormalities, especially spasms of blood vessels. Even without renal disturbances there may be nitrogen retention due to thirst and vomiting. The nitrogen content of the blood in cases of vomiting of pregnancy is a reliable index of the seriousness of the disease.

J. P. GREENHILL.

Evans, Arwyn: The Late Effects of Toxaemias of Pregnancy, J. Obst. & Gynec. Brit. Emp. **40:** 1024, 1933.

The author has investigated 76 albuminuric patients four months to four years after discharge from the Maternity Department of the Cardiff Royal Infirmary. Two-thirds of these were found to have after-effects, definite chronic nephritis being found in 12, probable chronic nephritis in 7, and simple albuminuria in 16 patients. However, 13 of the patients had other diseases present to account for the albuminuria. With regard to the remote prognosis the following conclusions were formed: (1) If albuminuria is present before the onset of labor for more than fourteen days, the possibility of chronic nephritis developing is very definitely increased. (2) A systolic blood pressure of 170 mm. Hg or over is dangerous, and when present for any length of time the question of terminating the pregnancy must be considered. (3) Every patient should remain in bed after the birth of the child until the albuminuria has disappeared, unless there is good reason to suppose that the chronic nephritis antedated the

pregnancy. (4) The older the albuminuric patient the more liable she is to develop after-effects. (5) The ultimate prognosis seems to be more favorable in primiparas than in multiparas. (6) A good prognosis may be given the child if he survives the first fourteen days. (7) The situation of the edema, the amount of albumin and presence or absence of casts in the urine do not seem to bear any relation to the remote prognosis.

WILLIAM F. MENGERT.

Gibberd, G. F.: The Significance of Recurrence in the Late Toxaemias of Pregnancy, J. Obst. & Gynec. Brit. Emp. **41**: 23, 1934.

One hundred and twenty-one women who suffered from a late toxemia of pregnancy were examined at intervals of from two to twelve years after the first toxemia. All of these 121 women were initially healthy, and none was included in the series unless there was positive evidence that she was free from renal disease prior to the first toxemic pregnancy. Thirteen of these 121 women, or 11 per cent, subsequently developed chronic nephritis, and 3 of them died of uremia. Thirty-five, or 38 per cent, had a recurrence of albuminuria with subsequent pregnancies but did not show evidences of permanent renal damage in the nonpregnant intervals.

The author concludes that a first toxemia may affect a previously healthy woman in one of three ways: It may give rise to an obvious chronic nephritis. It may be followed by a more or less habitual recurrence of the toxemia with subsequent pregnancies with apparently normal kidneys in nonpregnant intervals. It may leave the patient absolutely normal.

WILLIAM F. MENGERT.

Cadden, J. F., and McLane, Charles M.: A Study of Various Kidney Function Tests in Relation to the Toxemias of Pregnancy, Surg. Gynec. Obst. **59**: 177, 1934.

Chronic nephritis is a grave and fairly common complication of pregnancy, although it is one of the most difficult conditions to recognize in its earlier stages. Many tests have been developed for the purpose of detecting the impairment of kidney function. One of the difficulties of interpretation lies in the fact that all of the tests are not based on the same principle. A study has been made of the phenolsulphonephthalein, creatinine excretion, and urea clearance tests in 23 cases of normal pregnancy and in 343 women suffering from some type of toxemia. Only the urea clearance test is sufficiently sensitive to differentiate chronic nephritis from the other toxemias of pregnancy. The lower limit of normal is probably in the neighborhood of 70 per cent normal and the average urea clearance value is 75 and 68 per cent normal for antepartum and postpartum, respectively.

Fifty per cent of all the nephritic patients showed values below 70 per cent normal. There is no apparent relationship between blood pressure and kidney function as measured by the urea clearance test. According to this test, there is no kidney impairment in the low reserve kidney group.

The average urea clearance values for preeclampsia and eclampsia are lower than those obtained in normal pregnancy.

To be assured that one is dealing with a nephritic condition it is essential that repeated two-hour tests be performed.

WILLIAM C. HENSKE.

Picardi, Michele: The Use of Santonin in the Antitoxic Function of the Liver, Ginecologia (Torino) **1:** 227, 1935.

Picardi states that the antitoxic power of the liver is diminished during pregnancy. Such dysfunction, which is of moderate intensity in normal pregnancy, at term tends to disappear rapidly in the puerperium.

In the toxicosis of pregnancy this test notably shows a hepatic insufficiency in practically all of the cases and in some it was possible to establish a regular curve of elimination parallel to the improvement of the toxemia.

From the studies made with Santonin, the author was able to conclude that this new test for study of the hepatic function can also be used in the obstetric field with great advantage. Moreover, he states that additional to its practical value, it possesses marked simplicity.

AUGUST F. DARO.

Wodon, J. L.: The Experimental Production of Eclampsia by Means of Guanidine Intoxication, Rev. franç. de gynéc. et d'obstét. **30:** 72, 1935.

The author succeeded in producing eclamptic convulsions by the injection of guanidine. He found the same changes in the acid-base equilibrium of the blood as occurs in eclampsia. He considers this to support the hypothesis which attributes to alterations in the metabolism of guanidine an important rôle in the etiology of eclampsia.

J. P. GREENHILL.

Fauvet, E.: Eclampsia, a Hypophyseal Disorder, Arch. f. Gynäk. **155:** 100, 1933.

In this extensive and comprehensive study, the author shows that disturbances of water metabolism and balance and of the circulatory system predominate in the edematous, nephrotic and eclamptic syndromes which develop in pregnant and parturient women. The author was able to reproduce all these symptoms, except the convulsive seizures, by administering posterior pituitary extracts to animals.

The pregnant organism undergoes changes which are dependent upon increased hypophyseal function even in health. It is possible that labor is initiated by a hypophyseal hormone, although this is not proved. Anterior hypophyseal hormone is essential for lactation and for growth and development in the newborn. Hoffman and Anselmino have shown that the hypophysis controls the water balance and exchange, and blood pressure and that these substances are increased in eclamptics. Fauvet concludes that the eclamptic syndrome is produced by a pathologic hyperfunction of the hypophysis.

RALPH A. REIS.

Bickenbach, W., and Fromme, H.: Follicle Hormone Content in the Blood of Eclamptics, Klin. Wchnschr. **14:** 495, 1935.

The authors corroborated Heim's finding of marked increase of follicular hormone in the urine of eclamptic patients. Examinations of the blood of four eclamptic patients by the extraction method failed to reveal any noteworthy increase in follicular hormone over that found in normal pregnant women.

RALPH A. REIS.

Smith, Geo. Van S., and Smith, O. Watkins: Evidence for the Placental Origin of the Excessive Prolan of Late Pregnancy Toxemia and Eclampsia, Surg. Gynec. Obst. **61:** 175, 1935.

The serums of women with late pregnancy toxemia and eclampsia have been found to have the same effect upon the ovaries of hypophysectomized rats as the

serums of normally pregnant women. An extract of human placenta also had this effect, while hypophyseal prolan caused a follicular and luteal activity not caused by any of the other materials tested.

Quantitative analyses have shown that the placentas of toxemic and eclamptic patients contain excessive amounts of prolan and tend toward low levels of estrin as compared with the placentas of normal pregnancies.

Controls have shown that the liver, spleen, kidney, and fetus contain practically no prolan or estrin.

It is concluded that the excessive amounts of prolan previously reported in the blood and urine of toxemic and eclamptic women, as well as the tendency toward low levels of estrin, have their origin in the placenta.

A continued overproduction of prolan by the placenta is probably a related factor and possibly causal in the etiology of late pregnancy toxemia and eclampsia.

WILLIAM C. HENSKE.

Smith, George S., and Smith, O. Watkins: Further Quantitative Determinations of Prolan and Estrin in Pregnancy, Surg. Gynec. Obst. **61:** 27, 1935.

Quantitative studies of prolan and estrin in 27 cases confirm the previous findings of excessive gonad-stimulating hormone and subnormal levels of estrin in the toxemias of late pregnancy and eclampsia. They also show that an excess of prolan has probably been present for some time before the appearance of toxic symptoms in cases of late pregnancy toxemia. High levels of prolan during the sixth and seventh months in apparently normal women may indicate that toxemia will develop, whereas the finding of normal figures favors the prediction of continued normal pregnancy.

Although the highest values for serum prolan yet encountered have been in cases of eclampsia, the degree of excess of prolan does not always run parallel with the severity of the symptoms.

WILLIAM C. HENSKE.

Spiegler, R.: What Significance Has Galvanic Irritability in the Detection of Eclampsia? Monatschr. f. Geburtsh. u. Gynäk. **96:** 280, 1934.

The author found that galvanic irritability is increased during pregnancy, but it is markedly diminished in cases of toxemia. This diminution in electric irritability occurs so regularly that it may be considered an early symptom of eclampsia.

J. P. GREENHILL.

Hurwitz, David, and Bullock, L. T.: Failure to Find Pressor and Antidiuretic Substances in Patients With Toxemia of Pregnancy, Am. J. M. Sc. **189:** 613, 1935.

Blood was obtained from 1 eclamptic, 7 preeclamptics, 3 pregnant women with hypertension and chronic nephritis, and 3 nonpregnant patients with hypertension. Neither blood pressure raising nor antidiuretic substances were found in these bloods.

J. THORNWELL WITHERSPOON.

Spoljanskij, and Juzelevskij: The Cerebral Pressure in Eclampsia and the Question of Etiology of Convulsions, Monatschr. f. Geburtsh. u. Gynäk. **96:** 190, 1934.

Manometric measurements of the cerebral pressure in cases of eclampsia were found to be within normal limits. The normal pressure in the region of the cisterna magna in the reclining position goes up as high as 150 mm. water,

while in the sitting posture it is negative. An increase in pressure in the lumbar region does not always indicate an increase in cerebral pressure. A temporary chloroform anesthesia does not lower the cerebral pressure, but the pressure sinks in the region of the subarachnoid space when cerebral fluid is removed, regardless of the site of the withdrawal. The authors could find no confirmation of the theory that an increased intracranial pressure is the cause of eclamptic convulsions.

J. P. GREENHILL.

Eufinger and Weikersheimer: The Influence of Atmospheric Changes on the Incidence of Eclampsia, Arch. f. Gynäk. **154:** 15, 1933.

The greatest incidence of eclampsia at the Frankfurt Frauenklinik occurred during May and November. Temperature readings, humidity and barometric pressure apparently play no rôle in this series of eclamptic patients observed in a ten-year period. Sudden changes in temperature, however, are apparently causative factors in eclampsia, since 89 per cent of the eclamptic seizures took place on days with such sudden changes. It is probable that they affect the vegetative nervous system of preeclamptic patients and thus tend to throw such predisposed patients into eclamptic seizures.

RALPH A. REIS.

Tottenham: Seasonal Incidence of Eclampsia in Hong-Kong, Brit. M. J. **2:** 1067, 1933.

Eclampsia is thought to be more frequent in the hot countries and may be associated with an insufficient consumption of water by the patient. Tweedy shows a greater incidence (in Ireland) in cold and damp weather. Tottenham compares the incidence of eclampsia and severe albuminuria in the different months of the year at Hongkong (a semi-tropical place), the winter being cool and dry, and the summer hot and damp. Of the 97 cases reported, 66 occurred during the months of September to February inclusive (when the humidity is always below 80 per cent). From March to September (including the months June, July, and August which have the heaviest rainfall) eclampsia is decreased. However, in the 41 cases of severe albuminuria (other than eclampsia), the condition is perhaps more common in hot weather.

F. L. ADAIR AND IRA BROWN.

Brame, Dorthy D.: A Review of Eclampsia at The University of Virginia Hospital, Virginia M. Monthly **62:** 513, 1935.

This review covers the period 1925 to 1935, during which time 3,927 patients were seen. Of these, 112 had eclampsia, an incidence of 2.8 per cent of all labors, which is almost three times the incidence generally reported in textbooks. However, only three of these 112 patients had been seen in the prenatal clinic, which suggests that inadequate prenatal care is a factor in the unusual incidence of the disease in that institution. About 40 per cent of the patients were seen in the three spring months and 65 per cent of the patients were primiparas. The incidence of the three types of eclampsia was as follows: Antepartum, 74 per cent; intrapartum 8 per cent; postpartum 18 per cent. The maternal mortality was 15.1 per cent, and the infant mortality rate was 30 per cent. The maternal mortality rate was cut in half when more conservative therapeutic measures were used in the last two years. The cases were classified according to Eden, and it was found that the maternal mortality in the severe group was 30 per cent, in the mild group only 7 per cent.

EUGENE S. AUER.

Hauch, E., and Lehmann, K.: Investigations into the Occurrence of Eclampsia in Denmark During the Years 1918 to 1927, Acta obst. et gynec. Scandinav. **14:** 425, 1934.

In the entire country of Denmark during 1918 to 1927 there were 1,286 cases of eclampsia among 737,701 childbearing women, a frequency of 1 in every 571 cases. The authors could not detect any influence of the weather upon the incidence of eclampsia. They believe that primiparity plays a greater rôle than seasonal variations. They offer the same explanation for the great increase in the incidence of eclampsia among unmarried women. The disease seems to be more common among the youngest and oldest obstetric patients. The maternal mortality for the entire country was 15.5 per cent. The authors found that the mortality was influenced by the number of convulsions, the degree of albuminuria, and the height of the blood pressure.

The best results were obtained by means of expectant treatment. The mortality was highest in patients delivered by cesarean section. In the cases where convulsions occurred during labor the lowest maternal mortality was obtained by means of rapid delivery. Almost half of the children born were premature. The entire fetal mortality was 34.1 per cent.

J. P. GREENHILL.

Ross, Robert A.: The Toxemias of Pregnancy and Certain Deficiency Diseases. Virginia M. Monthly **62:** 424, 1935.

The author noted that in the area (rural North Carolina) from which his clinic practice mainly is drawn, eclampsia occurs most often in the same localities in which pellagra and similar vitamin deficiency diseases are frequently found. On close questioning he observed that the type of patients he saw in eclamptic convulsions subsisted mainly on a diet deficient in vitamin G (B_2), and also vitamins A, C, and D. Ross makes no conclusions from his observations except to state that the pellagra and eclampsia ratio is clearly parallel in North Carolina, and that he is trying to find a factor which may be helpful in the solution of the problem of the prevention of eclampsia.

EUGENE S. AUER.

Fauvet, E.: Clinical Aspects of Eclampsia, Arch. f. Gynäk. **157:** 139, 1934.

The author believes that abruptio placentae occurs secondarily to nephritis of pregnancy and may terminate fatally with signs of renal insufficiency. In two patients the maximum excretion of urine and rise in blood pressure did not occur for two weeks after delivery. This may have resulted from secondary inflammatory edema of the kidneys. The anuria may be due to compression of the renal parenchyma, and Fauvet believes that the hypertension is an attempt to overcome this compression. The administration of fluids may be a life-saving measure if this compensatory action fails. Such treatment is successful only in threatening anuria as a result of kidney edema. It is not advisable in circulatory failure.

Fauvet also discusses the causes of late puerperal hypertension and believes that this is due to hormonal action of the hypophysis-interbrain system.

RALPH A. REIS.

Correspondence

A Proposed Obstetric Term

To the Editor:

I hesitate to introduce another term to the obstetric profession, but I feel there is a place for the term "incitoduction." It is especially valuable for use by the record librarian.

The term "induction of labor" should be confined to the patient who is not in labor at the time drugs or mechanical means are employed to bring the patient into labor.

The term "incitoduction" could be applied and should be confined to the use of drugs or mechanical means to stimulate labor in a patient who is already in labor.

Under the present classification we have no place nor a term to index this type of patient. We do not really induce labor in these patients, since labor is already started. What we do is to accelerate the time of delivery.

The verb incite is defined as follows: "to impel to a particular action; urge onward," while the verb induce is defined: "to influence to an act; to lead to or produce." Therefore the term "incitoduction" can be very nicely used to indicate that we hasten the time of delivery of a woman either by drugs or mechanical means.

EDWARD LYMAN CORNELL, M.D., F.A.C.S.
Chicago, Ill.

Item

American Board of Obstetrics and Gynecology

The next written examination and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology will be held in various cities in the United States and Canada on Saturday, November 7, 1936.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Bldg., Pittsburgh (6), Pennsylvania. Applications for this examination should be filed in the Secretary's Office sixty days prior to the scheduled date of examination.

Erratum

In Dr. Stein's discussion of Dr. Irving's paper in the July issue, page 48, the first line should read: "At the Michael Reese Hospital," instead of "At the Cook County Hospital."